

NON-SURGICAL CONTRACEPTION IN FEMALE DOGS AND CATS

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Abstract. Gonadectomy is the most commonly used method for permanent contraception in small animals. The irreversibility of the method is however a main drawback for its use in valuable breeding animals. Moreover, several negative side effects can be observed after surgical castration. Therefore several non-surgical methods were developed. This paper describes the current non-surgical methods of contraception used in female dogs and cats. They include hormonal procedures, such as application of progestins, androgens and GnRH analogues in order to prevent the ovarian cycle. Another method is the use of 4-vinylcyclohexene diepoxide, an industrial chemical destroying primordial and primary ovarian follicles. Further prospective possibilities consist in immunocontraception and in the elaboration of a safe and effective vaccine with reversible effect. Finally the use of several abortive drugs, such as aglepristone, PGF₂ α and dopamine agonists are presented.

Key words: dog, cat, female, non-surgical contraception, oestrus prevention

INTRODUCTION

Surgical contraception by gonadectomy (castration) is frequently instituted in animals of both sexes and provides a permanent and irreversible effect. Additionally it may also serve as a method for treating diseases of the reproductive tract or hormone-dependent disorders. Finally gonadectomy may prevent sexually spread

diseases such as Sticker venereal tumor in dogs. On the other hand, it is also important to take into account the possible side effects of castration such as underdevelopment of genital organs, disturbances in the musculoskeletal system, hormonal dysfunctions, urinary incontinence, risk of neoplasms, obesity, coat changes, etc. [Root Kustritz 2007, Reichler 2009, Root Kustritz 2012]. An alternative method is non-surgical contraception which may be either permanent or temporary. When choosing for one of both methods, it is necessary to consider the expected benefits and potential risks. Not only the availability of particular procedures or drugs, but also individual circumstances, such as the exact purpose (especially the duration of contraceptive effect), the potential impact on future fertility, medical contraindications and potential adverse side effects and ethical problems should be taken into account.

The aim of this article is to present the current methods of contraception in female dogs and cats in terms of their effectiveness and safety.

PROGESTINS

For decades, various formulations of this group of drugs were extensively used for contraception of female dogs and cats. Their mechanism of action is similar to that of endogenous progesterone [Conneely *et al.* 2003, Romagnoli and Concannon 2003, Mulac-Jericevic and Conneely 2004]. The steroid hormone passes through the cell membrane into the cell, and its biological activity is initiated after binding with the progesterone receptor isoforms PR-A and PR-B [Conneely *et al.* 2003]. The presence of progesterone receptors was confirmed *inter alia* in the uterus, mammary gland, central nervous system and pituitary gland. The basic mechanism of progestagenic action is a reduction in the pulse frequency of gonadotropin-releasing hormone (GnRH) secretion, thus inhibiting follicle-stimulating hormone (FSH) and luteotropic hormone (LH) secretion and cessation of follicular development and maturation [Colon *et al.* 1993, Romagnoli and Concannon 2003]. Progestins are most effective in inhibiting the sexual cycle when administered during the period of ovarian inactivity (*i.e.* anoestrus). The most frequently used progestins include medroxyprogesterone acetate, megestrol and proligeston. Less known or currently less frequently used are delmadinone acetate, chlormadinone and norethisterone [Jurka and Max 2006]. Melengestrol acetate and levonorgestrel were experimentally investigated in dogs and cats, but they are currently not extensively used in small animal practices [El Etreby 1979, Romagnoli and Concannon 2003]. Most of the mentioned progestins are active when given orally as well as parenterally. Progesterone itself is not used as a contraceptive agent because of its poor bioavailability after oral application. Administered by injection it has a short half-life of a few days. The hormone is sometimes

effectively used for maintenance of pregnancy when a deficiency of endogenous progesterone is taking place [Jurka and Max 2006].

Medroxyprogesterone acetate (MPA) belongs to the old generation of contraceptive agents. It is characterized by high antigonadotropic and gestagenic activity, but shows a relatively small antiestrogenic effect [Evans and Sutton 1989, Berky and Townsend 1993]. It is slowly metabolised in the liver. After a single administration during the pro-oestrus MPA blocks the oestrous cycle for on average 6 months. However, a lack of heat was also described in some bitches up to 26 months after application. For this reason MPA administered parenterally should not be used in valuable breeding animals. When administered orally, this compound is effective for suppression of heat during pro-oestrus as well as for temporary postponement of heat. However, due to the potential side effects, this substance is not approved for use in several countries such as the United States. Megestrol acetate (MA), similarly to MPA, is considered to be one of the older generation of drugs with high gestagenic and antigonadotropic activity but poor anti-estrogenic effects. This compound has a shorter working time than MPA and is additionally approved in many countries. This progestin shows less side effects than MPA and can be administered orally in dogs and cats [Jurka and Max 2006]. A more recently developed progestin is proligestone (PROL) which activity is mainly antigonadotropic, and to a lesser extent, gestagenic and antiestrogenic. This reduces the side effects to the uterus and mammary glands [Bertchold 1986, Berky and Townsend 1993, Fieni et al. 2001]. When used in the pro-oestrus in order to stop the heat, it should be administered intramuscularly because of a better clinical effect. However, administration of a progestin during this period involves important risks due to the possible development of endometritis. For long-term postponement of the oestrus PROL is used in the injectable form, preferably during the anoestrus phase in intervals of 3 months, subsequently 4 months and finally every five months. After a single injection heat is prevented for a period of 3 to 9 months. An overview of the different progestagenic formulations with indication of manufacturers is summarized in Table 1.

The use of exogenous progestins however is associated with several important side effects [Max and Jurka 2006 a]. These are most frequently observed in the uterus, such as endometrial cystic degeneration, also referred to as CEH – cystic endometrial hyperplasia [De Cock et al. 2002, Kim and Kim 2005, Keskin et al. 2009]. While estrogens stimulate progesterone receptors in the endometrium, progesterone and synthetic progestins stimulate uterine glands to secretion, causing hyperplasia and hypertrophy, and consequently the formation of cysts of various sizes, which often is accompanied by infiltration of leukocytes. Prolonged secretory activity in combination with infection of the uterine cavity (especially in immunocompromised animals), may lead to the development of endometri-

Table 1. Progestin drugs for contraception of female dogs and cats
 Tabela 1. Preparaty progestagenowe w antykoncepcji u suk i kotek

Permanent blocking of heat Trwała blokada cyklu		Postponement of heat Przesunięcie rui			Suppression of heat* Przerwanie rui*	
Bitch – Suka	Queen – Kotka	Bitch – Suka	Queen – Kotka	Bitch – Suka	Queen – Kotka	Queen – Kotka
Covinan; Delvosteron (proligeston 100 mg/ml) Dosage: 10–33 mg/kg. First injection given during <i>anoestrus</i> , the second after 3 months, the third after 4 months and subsequent injections at 5 monthly intervals. Dawka: 10–33 mg/kg. Pierwsza iniekcja podawana w <i>anoestrus</i> , druga po upływie 3 mies., trzecia po upływie kolejnych 4 mies. i następne dawki co 5 mies.	Covinan; Delvosteron (proligeston 100 mg/ml) Dosage: 100 mg pro animal. First injection given during <i>anoestrus</i> , the second after 3 months, the third after 4 months and subsequent injections – at 5 monthly intervals. Dawka: 100 mg/zwierzę. Pierwsza iniekcja podawana w <i>anoestrus</i> , druga po upływie 3 mies., trzecia po upływie kolejnych 4 mies. i następne dawki co 5 mies.	Covinan; Delvosteron (proligeston 100 mg/ml) Dosage: 20–30 mg/kg. A single injection given 2–3 weeks before the expected <i>pro-oestrus</i> . The subsequent <i>pro-oestrus</i> will occur on average 6 months after the injection Important! A heat can occur in the case of too late drug administration. Dawka: 20–30 mg/kg. Podanie jednorazowe na 2–3 tygodnie przed spodziewaną ciezką. Kolejna ruja zwykle występuje po 6 miesiącach. Ważne! Cieczka może wystąpić w przypadku zbyt późnego podania leku.	Covinan; Delvosteron (proligeston 100 mg/ml) Dosage: 100 mg pro animal. A single injection given 3 weeks before the expected heat. Dawka: 100 mg/zwierzę. Podanie jednorazowe na około 3 tygodnie przed spodziewaną rują.	Covinan; Delvosteron (proligeston 100 mg/ml) Dosage: 10–33 mg/kg. A single injection given at the start of <i>pro-oestrus</i> . Usually the heat returns after 3–12 months** Important! The substance is absorbed slowly; within 7 days after administration the bitch may still be fertile. Dawka: 10–33 mg/kg. Ruja powraca zwykle po 3–12 mies.** Ważne! Preparaty wchłaniają się wolno; przez 7 dni po podaniu suka może być jeszcze płodna.	Covinan; Delvosteron (proligeston 100 mg/ml) Dosage: 100 mg/pro animal. A single injection given at the start of heat. Dawka: 100 mg/zwierzę. Podanie jednorazowe na początku rui.	Covinan; Delvosteron (proligeston 100 mg/ml) Dosage: 100 mg/pro animal. A single injection given at the start of heat. Dawka: 100 mg/zwierzę. Podanie jednorazowe na początku rui.
Depo-Promone; Promone-E (medroxyprogesterone acetate 50 mg/ml)	Depo-Promone; (medroxyprogesterone acetate 50 mg/ml)	Provera (medroxyprogesterone acetate tablets 5 and 10 mg)	Provera (medroxyprogesterone acetate tablets 5 and 10 mg)	Provera (medroxyprogesterone acetate tablets 5 and 10 mg)	Provera (medroxyprogesterone acetate tablets 5 and 10 mg)	Provera (medroxyprogesterone acetate tablets 5 and 10 mg)

cont. Table 1 – cd. tabeli 1

	Permanent blocking of heat Trwała blokada cyklu			Postponement of heat Przesunięcie rui			Suppression of heat* Przerwanie rui*		
	Bitch – Suka	Queen – Kotka	Bitch – Suka	Queen – Kotka	Bitch – Suka	Queen – Kotka	Bitch – Suka	Queen – Kotka	Queen – Kotka
acetate 50 mg/ml)									
Dosage for dogs weighing up to 45 kg: 50 mg pro animal; over 45 kg 75–100 mg pro animal. First injection given in <i>anoestrus</i> . Subsequent injections – at 4 monthly intervals. Important! After 1.5 years it is recommended to stop the administration for a period of 2–3 months. Dawka: 50 mg/zwierzę. Kolejne dawki co 4 miesiące. Ważne! Po upływie 1,5 roku zaleca się przerwać podawanie na okres 2–3 miesięcy. Dawka dla suk o masie ciała do 45 kg: 50 mg/zwierzę; powyżej 45 kg 75–100 mg/zwierzę. Pierwsza iniekcja podawana w <i>anoestrus</i> . Następne iniekcje co 6 mies. Ważne! Nie stosować dłużej niż 2,5 roku. Nie stosować u suk hodowlanych.	Dosage: 50 mg pro animal. Subsequent injections – at first dose given 10 days before the expected <i>pro-oestrus</i> . Continue for some days in order to short-term postpone the heat. The heat is expected within 4–5 days after the cessation of drug administration. Dawka: 50 mg/zwierzę. Kolejne dawki co 4 miesiące. Ważne! Pierwsza dawka na 10 dni przed spodziewaną cieczką. Podawać przez kilka dni w celu krótkotrwałego przesunięcia rui. Spodziewana cieczka w czasie 4–5 dni od zaprzestania podawania leku.	Dosage: 5 mg/day pro animal. Repeat for some days. The heat is expected within some days or even months after the cessation of drug administration. Dawka: 2,5 mg/zwierzę /dzień. Podawać przez kilka dni. Powrót rui po kilku dniach, a nawet miesiącach od zaprzestania podawania leku.	Dosage: 5 mg/day pro animal. The first dose given 10 days before the expected <i>pro-oestrus</i> . Continue for some days in order to short-term postpone the heat. The heat is expected within 4–5 days after the cessation of drug administration. Dawka: 5 mg/zwierzę /dzień. Pierwsza dawka na 10 dni przed spodziewaną cieczką. Podawać przez kilka dni w celu krótkotrwałego przesunięcia rui. Spodziewana cieczka w czasie 4–5 dni od zaprzestania podawania leku.	Dosage: 2,5 mg/day pro animal. Repeat for some days. The heat is expected within some days or even months after the cessation of drug administration. Dawka: 2,5 mg/zwierzę /dzień. Podawać przez kilka dni. Powrót rui po kilku dniach, a nawet miesiącach od zaprzestania podawania leku.	Dosage for dogs weighing up to 25 kg: 10 mg pro animal for 3 days, then 5 mg pro animal for subsequent 12–14 days; over 25 kg: apply double doses. Signs of heat disappears within 3–4 days. Dawka dla suk o masie ciała do 25 kg: 10 mg/zwierzę przez 3 dni, potem 5 mg/zwierzę przez kolejne 12–14 dni. U suk o masie ciała powyżej 25 kg stosować podwójne dawki. Objawy rui ustępują po 3–4 dniach.	Dosage: 5 mg/day pro animal for 4 days, then 2,5 mg pro animal for subsequent 14 days. Dawka: 5 mg/zwierzę/dzień przez 4 dni, następnie połowa tej dawki przez kolejne 14 dni.			

cont. Table 1 – cd. tabeli 1

Permanent blocking of heat Trwała blokada cyklu		Postponement of heat Przesunięcie rui		Suppression of heat* Przerwanie rui*	
Bitch – Suka	Queen – Kotka	Bitch – Suka	Queen – Kotka	Bitch – Suka	Queen – Kotka
Perlutex (medroxyprogesterone acetate tablets 5 mg) Dosage: 2.5–3.0 mg/kg. For dogs weighing up to 15 kg: 2 tablets daily for 4 days, then 1 tablet daily for 2 weeks; over 15 kg apply double doses. The first dose given in <i>anoestrus</i> . Dawka: 2,5–3,0 mg/kg. Suki o masie ciała do 15 kg: 2 tabletki dziennie przez 4 dni, potem 1 tabl. dziennie przez 2 tygodnie. Suki o masie ciała powyżej 15 kg: podwójne dawki. Pierwsza dawka podawana w <i>anoestrus</i> .	Perlutex (medroxyprogesterone acetate tablets 5 mg) Dosage: 1 tablet pro animal given weekly. Dawka: 1 tabletka na zwierzę podawana raz w tygodniu.	Promon Vet (medroxyprogesterone acetate tablets 5 mg) Dosage: 5 mg/day pro animal. The first dose given 10 days before the expected <i>pro-</i> <i>oestrus</i> . Continue for some days in order to short-term postpone the heat. The heat is expected within 4–5 days after the cessation of drug administration. Dawka: 5 mg/zwierzę/dzień. Zacząć podawać na 10 dni przed spodziewaną ciezką. Podawać przez kilka dni w celu krótkotrwałego przesunięcia rui. Spodziewana cieczka w czasie 4–5 dni od zaprzestania podawania leku.	Promon Vet (medroxyprogesterone acetate tablets 5 mg) Dosage: 2.5 mg/day pro animal. Continue for some days. The heat is expected within some days or even months after the cessation of drug administration. Dawka: 2,5 mg/zwierzę/dzień. Podawać przez kilka dni. Powrót rui po kilku dniach, a nawet miesiącach od chwili zaprzestania podawania leku.	Promon Vet (medroxyprogesterone acetate tablets 5 mg) Dosage for dogs weighing up to 25 kg: 10 mg pro animal for 3 days, then 5 mg pro animal for subsequent 12–14 days; over 25 kg apply double doses. Signs of heat disappears within 3–4 days. Dawka u suk o masie ciała do 25kg: 10 mg/zwierzę przez 3 dni, potem 5 mg/zwierzę przez kolejne 12–14 dni. U suk o masie ciała powyżej 25 kg stosować podwójne dawki. Objawy rui ustępują po 3–4 dniach.	Promon Vet (medroxyprogesterone acetate tablets 5 mg) Dosage: 5 mg/day pro animal for 4 days, then the half dose for subsequent 14 days. Dawka: 5 mg/zwierzę /dzień przez 4 dni, następnie połowa tej dawki przez kolejne 14 dni.

cont. Table 1 – cd. tabeli 1

Permanent blocking of heat Trwała blokada cyklu		Postponement of heat Przesunięcie rui		Suppression of heat* Przerwanie rui*	
Bitch – Suka	Queen – Kotka	Bitch – Suka	Queen – Kotka	Bitch – Suka	Queen – Kotka
Depogeston (medroxyprogesterone acetate 50 mg/ml) Dosage for dogs weighing up to 10 kg: 1 ml pro animal; 10–45 kg: 1.5–2.0 ml pro animal.	Depogeston (medroxyprogesterone acetate 50 mg/ml) Dosage: 50 mg (1 ml) pro animal. Dawka: 50 mg (1 ml) /zwierzę.				
The first dose given in <i>anoestrus</i> .					
Dawka dla suk o masie ciała do 10 kg: 1 ml/zwierzę. U suk od 10– 45 kg: 1,5–2,0 ml/zwierzę. Pierwsza dawka podawana w <i>anoestrus</i> .					

* in authors' opinion the procedure is risky – w opinii autorów postępowanie ryzykowne.

** sometimes the heat is stopped for a longer time – nieraz ruja zostaje wstrzymana na dłuższy czas.

tis/pyometra complex. Furthermore, in dogs and cats mammary tumors, hyperglycemia and acromegaly were observed after repeated progestin administrations. Progestins can stimulate local secretion of growth hormone by the mammary glands, inter alia, via insulin-like growth factor IGF-1, which induces proliferative processes [Mol et al. 1996]. One of them is feline fibroadenomatosis, the rapid, but not malignant, proliferation of cells in the ducts and stroma of the mammary glands which is considered to be hyperplastic/dysplastic changes. The condition may be a result of natural progestin activity and sometimes arises in cats treated with progestins, especially long-acting formulations [Jurka and Max 2009]. Other possible side effects are adrenal dysfunction, hepatitis, developmental disorders, withholding of labor, behavioral changes and local skin alterations. Simultaneously with a decrease in the concentration of the administered progestin and the increase in prolactin secretion, signs of pseudopregnancy may be observed.

ANDROGENS

Preparations of this group are widely used for female contraception. The use of injectable or oral testosterone derivatives prevent oestrus in females. The synthetic androgen mibolerone exists in the form of a commercial oral preparation (Cheque Drops) for dogs and cats in the United States. The formulation is characterized by anabolic and antigonadotropic activity of the hormone. If the treatment is implemented at least 30 days before the start of a pro-oestrus, the heat is suppressed. The treatment can be continued for two years. Longer administration is not recommended because of possible hepatotoxicity. After discontinuing, the subsequent oestrus occurs in a period of 1 to 7 months with an average of 70 days [Kutzler and Wood 2006]. The drug is contraindicated in animals suffering from tumors in the anal region and in Bedlington terriers due to a genetic defect often leading to chronic hepatitis in this breed. In cats, the effective dose is slightly lower than the toxic one, thus mibolerone is contraindicated in this species. This group of drugs is however not approved for use in Europe.

GnRH AGONISTS – SUBCUTANEOUS IMPLANTS

GnRH (gonadoliberin) – a hormone produced by the hypothalamic region induces the release of gonadotropins from the pituitary gland. After a long period of GnRH administration, the preovulatory LH surge appeared to be lower than in undisturbed cycles. This could be explained by the decrease of pituitary gland sensitivity in those animals as a result of continuous exposure to gonadotropin releasing hormone. Consequently the idea appeared to use synthetic GnRH ana-

logues – agonists (providing the same biological effect as the natural hormone) in the form of subcutaneous implants, from which the active substance is released slowly and constantly over a long period of time. This ensures the maintenance of an appropriate blood hormone concentration and its expected activity, i.e. reduction of GnRH receptor content (down-regulation) in the pituitary cells. This mechanism inhibits the secretion of gonadotropins, suppressing ovarian activity [Cathey and Memon 2010]. Studies using GnRH agonists reported a simultaneous decrease in testes size and consistency [Fontaine and Fontbonne 2011].

As an adverse reaction a flare-up effect is frequently observed. It consists in the fact that initially an ovarian stimulation occurs (i.e. appearance of heat) while after a prolonged period of GnRH analogue activity the suppressive effect starts. This initial stimulatory effect is more often observed when the implant is applied during the anoestrus phase in comparison to application during the dioestrus phase. Therefore the phase of luteal activity lasting about two months after the heat (i.e. the dioestrus) is recommended as the most appropriate for the first introduction of the implant.

In 2006 an implant containing nafarelin at a dose of 18.5 mg, called Gonazon, was introduced on the European market. This compound is inserted in the umbilical region in dogs, and in the neck in cats. The implant is not recommended for breeding females because of the long and variable duration of the contraceptive activity and ovulation disorders often occurred during the first oestrus period after cessation of action. Additionally, it is not recommended for use in females before puberty, because stopping the secretion of gonadal steroids may predispose to vaginitis. Another formulation of GnRH agonist is marketed as the implant Suprelorin comprising of a GnRH analogue, named deslorelin. Its activity is similar to what is described above, but currently it is only registered for temporary chemical castration of male dogs. Off-label use has shown that the drug can also be used for long-term prevention of heat in female dogs. However, frequently an initial heat is observed shortly after the implant is inserted due to the flare-up effect [Fontaine et al. 2011].

According to Toydemir et al. [2012] 9.5 mg deslorelin implants successfully suppressed estrus behaviour and estradiol secretion in queens for at least 18 months. Microscopic findings of the ovaries confirmed their inactivity. Inactive gonads had similarities with the normal juvenile feline ovary exhibiting high numbers of primordial and primary follicles, a few small antral and some atretic antral follicles. Deslorelin at a dose of 4.7 mg blocked the feline ovarian cycle for 8 to 12 months. Implant insertion during the heat allowed to avoid the flare-up effect [Jurka and Kacprzak 2013].

Deslorelin implants may also be used to postpone puberty in queens. The implant should be placed when the female has reached 50% of the body weight. The treatment did not influence the growth rate [Risso et al. 2012].

GnRH ANTAGONISTS

The working mechanism of these agents consists in binding to GnRH receptors and therefore stopping the action of endogenous GnRH. This suppresses gonadotropins secretion and blocks the ovulation without initial stimulatory effect. When given to pregnant bitches it can induce abortion which is not the case in queens [Gobello 2012]. Currently there are however no registered formulations of this group on the veterinary market.

4-VINYLCYCLOHEXENE DIEPOXIDE (VCD)

The substance was investigated by medical researchers using rodent models. Repeated exposure to VCD selectively destroys primordial and primary follicles by increasing the rate of follicular atresia by apoptosis [Springer et al. 1996, Fagerstone et al. 2010]. In an experiment significant or near-complete depletion of the ovarian oocyte pool was demonstrated in mice and rats [Hoyer et al. 2001]. ContraPest containing VCD was prepared to reduce the brown rat population in urban areas. This chemosterilant causes a destruction of primordial and primary ovarian follicles, leading to the total and permanent infertility in dogs and cats [Cathey and Memon 2010]. It can be administered parentally and orally. The commercial product, ChemSpay was registered in the United States in 2010.

IMMUNOCONTRACEPTION

For a long time attempts are exerted to use immunological phenomena for contraception in animals. The main idea consists in the induction of antibodies directed against antigens playing an important role in reproduction. An antigen–antibody reaction should lead to infertility lasting as long as a sufficiently high level of specific antibodies exists in the blood circulation. The main problem however is the choice of suitable antigen characterized by adequate immunogenicity in order to achieve a contraceptive vaccine [Munks 2012].

Zona pellucida antigens

The zona pellucida is a non-cellular glycoprotein membrane covering the oocyte and (after fertilization) the embryo up to the late blastocyst stage, whereupon it breaks and disappears. Three major zonal glycoproteins with different molecular weight designated as ZP1, ZP2 and ZP3 have been isolated from the membrane. Apart from its structural function the zona pellucida is of great functional importance. It contains sperm receptor sites, which allow fertilization. Antizonal antibodies do not allow fertilization, without affecting the hormonal activity. Experiments were conducted in dogs and cats by using both allogeneic or xenogeneic zonal antigens, in particular derived from swine oocytes, which are easy to obtain because of wide availability of fresh slaughter material. Also recombinant antigens, obtained by biotechnological methods were used [Gorman et al. 2002, Srivastava et al. 2002, Levy et al. 2005, Eade et al. 2009]. Uncertain contraceptive efficacy, especially in cats, does not entitle to introduce this method to the daily small animal practice at this moment.

GnRH antigens

Immunization with GnRH antigens was performed in order to obtain specific antibodies binding natural GnRH [Robbins et al. 2004, Samoylov et al. 2012]. The results have shown high contraceptive effectiveness in cats, of which 93% remained infertile for one year after immunization, while after 2, 3 and 4 years post immunization 73, 53 and 40% of the animals respectively were still sterile [Levy et al. 2011]. In the U.S. a contraceptive vaccine called GonaCon is marketed and since 2009 it is approved for use in order to reduce the animal population of certain species of free-living animals. Registration of the vaccine is expected also for the free-living dogs, perhaps administered in conjunction with rabies vaccination [Bender et al. 2009].

LH receptor antigens

The essence of the action of LH receptor antigens is to cause the production of antibodies that bind to LH receptors (LH-R), what prevents the biological activity of luteinizing hormone and indirectly inhibits the physiological activity of the ovaries. Bitches and queens were immunized effectively using bovine LH-R [Saxena and Perkins 2002, Saxena et al. 2003]. Currently there are however no commercial products available.

PHARMACOLOGICAL TERMINATION OF PREGNANCY

A special form of contraception is the termination of diagnosed or putative pregnancy. Reasons for such treatment arise from the animal owner's decision (unwanted pregnancy) or medical indications. Among them are intractable diseases related to pregnancy or other illness, at which pregnancy becomes a threat to the female's life. They include metabolic disorders (gestational diabetes, ketosis, hypocalcemia) and renal failure. Termination of pregnancy can be performed by surgery (ovariohysterectomy) or pharmacologically. So far formulations used for this purpose include glucocorticoids, PGF 2α and dopamine agonists (cabergoline, bromocriptine, metergoline), or combinations of these drugs. Especially the dopamine agonists tend to be effective, despite the lack of registration for this indication. Currently, however, the most frequently used abortive agent is aglepriston, a progesterone receptor blocking agent (Alizine, Virbac). The drug used in doses of 10 mg · kg $^{-1}$ in bitches and 15 mg · kg $^{-1}$ in queens (administered twice with 24-h interval) is highly effective with no or minimal side effects [Fieni et al. 2006, Max and Jurka 2006 b]. The pregnancy termination usually occurs within a few days after the start of the treatment. Regardless of the agent used the pregnancy and induction of abortion should be monitored carefully to avoid unexpected birth due to survival of one of the fetuses.

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NIECHIRURGICZNE METODY ANTYKONCEPCJI U SAMIC PSÓW I KOTÓW

Streszczenie. Gonadektomia (kastacja) jest najbardziej rozpowszechnioną metodą trwałej antykoncepcji u małych zwierząt. Jednak wadą tej metody jest jej nieodwracalność, co czyni ją nieprzydatną dla wartościowych zwierząt hodowlanych. Ponadto po chirurgicznym usunięciu gonad obserwuje się niekorzystne skutki uboczne. Rozwijają się zatem niechirurgiczne metody antykoncepcji. W artykule przedstawiono współczesne metody antykoncepcji niechirurgicznej u samic psów i kotów. Obejmują one postępowanie hormonalne, takie jak stosowanie progestagenów, androgenów i analogów GnRH w celu blokowania cyklu jajnikowego. Inną metodą jest użycie diepoksydu 4-winylocykloheksanu, związku chemicznego wykorzystywanego w przemyśle, który uszkadza pęcherzyki jajnikowe pierwotne i pierwszorzędowe. Istnieją też możliwości antykoncepcji immunologicznej polegającej na opracowaniu bezpiecznej i skutecznej szczepionki antykoncepcyjnej o działaniu odwracalnym. Na końcu omówiono wybrane środki poronne, takie jak aglepriston, PGF 2α i agoniści dopaminy.

Słowa kluczowe: pies, kot, samica, antykoncepcja niechirurgiczna, zapobieganie ru

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