



ABSTRACTS

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SURGICAL CONTRACEPTION: PROS AND CONS

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Contraception by surgical sterilization or gonadectomy is usually an irreversible intervention resulting in a permanent cessation of the reproductive function. Surgical methods where the gonads are removed, are ovariectomy (OVE) or ovariohysterectomy (OVH), through the linea alba (traditional midline ovariohysterectomy), through the flank (lateral flank ovariohysterectomy) or by laparoscopy.^{1,2} In contrast to the removal of the gonads the sterilisation by means of a vasectomy, salpingectomy (tubal ligation) and hemiovariohysterectomy (leaving one ovary in place) also results in the elimination of reproductive function, but the sexual behaviour and the incidence of diseases transmitted by sexual hormones is not influenced.

History - The first comments concerning the neutering of dogs and cats are found in the Mosaic laws (about 600 B.C.). Apart from eliminating the reproductive function of dogs and cats, gonadectomy was also performed to suppress sexual behavior, as shown by documents from the 18th and 19th century. When an Italian women was asked by her French friend, what she was going to do with a neutered cat, she answered: „Lo tengo per non guastarmi la vita (I keep him so to facilitate my life).³ In the middle of the 19th century female dogs were also spayed to save their owners troubles.⁴

Social and cultural influences - In Germany and Switzerland the main reason for neutering has always been to make the keeping of dogs easier. Male dogs are predominantly neutered to treat behavioral problems (69%). Neutering female dogs is predominately linked to simplifying handling for the owner (51%) and to preventing diseases and reproduction (36%).⁵ To the author's knowledge, no data evaluating the reasons to neuter queens and tomcats are available. However, in cats kept as pets, the prevention of reproduction in queens and the specific sexual behaviors, such as urine spraying in tomcats, are the most likely reasons.

The request for gonadectomy is affected by cultural influences, as seen in the differing numbers of neutered male and female dogs in different countries (see table 1). These differences cannot be attributed only to the owner, but also to the advice of the veterinarian. One clear example is the treatment of prostate hyperplasia. In Germany, castration of male dogs is the treatment of choice for prostate hyperplasia, whereas in France, this treatment is regarded as the last option.⁶

Table 1: Dog population and frequency of gonadectomy

	France	Spain	Germany	Switzerland
Dog population	8,508 000	4,510 0000	6,473 0000	480 000
Spayed females	25%	18%	28%	62%
Neutered males	12%	6%	25%	32%

Gonadectomy to control pet overpopulation

Until now, gonadectomy is the contraceptive technique of choice. Because gonadectomy is irreversible, spay programs are widely accepted for population control. In spite of worldwide efforts to reduce pet overpopulation, the number of dogs and cats is still increasing. A study by the AVMA found that in the USA, despite intensively promoted contraception (76% of privately owned dogs and 83% of cats were neutered) and the destruction of pets (5 million

dogs and cats were killed per year), each year the dog population increases by 3.5% and the cat population by 2.9%.⁷

Similar data exist for Europe. In Berlin, over a period of more than 10 years, between 5,000 and 10,000 stray cats were captured, neutered and released, but with no observable lasting effect. The analysis of Berlin shows that even if two thirds of the female cats are spayed there will still be an increase in the cat population. If all female cats of an individual population are spayed, then foreign cats will immigrate.⁸ Castration and death of tomcats had no effect on the total number of the whole population, because foreign tomcats migrated and the number of adult tomcats remained the same over the observation period. In 1977 Wildt made the statement: "It is therefore generally agreed that this program (spay program) is only an adjunct to the total overpopulation solution".⁹ He also emphasized: „There is no way to know how much more severe the problem would be today, if spaying had not been widely practiced."

Researchers across the planet are searching for a single and simple contraceptive method which will result in the permanent elimination of reproduction, but which would be significantly less costly than neutering. In male dogs this can be achieved by the intratesticular injection of zinc gluconate. However, whether the goal of reproductive control in the polygamous species dog can be achieved by the „reproductive elimination“ of male dogs alone remains to be seen. Studies showed that the territorial behavior of castrated tomcats is less pronounced, therefore intact tomcats migrate into this territory and the reproductive rate remains the same.⁸ In contrast to gonadectomy, the intratesticular injection of male adult dogs with zinc gluconate results in infertility without an effect on the sexual territorial behavior. As a result, a long-term effect may then still be possible if not all male dogs are sterilized.

Until something more suitable becomes available, the spaying of female dogs and cats is still recommended to avoid high population densities, animal suffering and the spread of zoonosis. The castration of tomcats is also recommended, because castrated cats have on average better health and a reduced mortality rate when compared to intact cats.⁸

The necessity, and in particular the timing, of gonadectomy in dogs and cats kept as pets is still controversial. This is mainly because gonadectomy confers a mixture of benefits and adverse affects depending on age at neutering, sex, species and breed. Therefore, Spain claims: "Any policy decision should consider the frequency and consequences of any condition".¹⁰

Effect of spaying on the reproductive tract - In some countries, ovariohysterectomy (OVH) is the preferred technique for spaying dogs. This preference was most likely based on the presumption that future uterine pathology is prevented by removing the uterus. However, historical reviews of the short-term and long-term complications after OVH and ovariectomy (OVE) leads to the conclusion that there is no benefit and thus no indication for removing the uterus during routine neutering in healthy bitches.^{11,12} At our clinic OVH is only performed in older bitches or bitches treated with gonadal steroids.

With the removal of the gonads, diseases such as ovarian tumors and cysts cannot occur. Furthermore, spayed dogs and cats are no longer susceptible to disorders mediated by ovarian hormones such as vaginal hyperplasia or metropathies. In spayed dogs and cats metropathies are virtually non-existent, whereas it is common in intact or progestagen treated animals. In Sweden approximately 7% of all bitches are spayed and a study showed that almost 25% of all registered dogs up to 10 years of age developed a pyometra.¹³ In addition, in 5 year old queens there was a significant likelihood of clinical evidence for uterine disease.¹⁴ OVH is then the recommended treatment of choice despite reported mortality rates are as high as 17% in dogs^{15,16} and 8% in cats^{16,17}.

Effect of gonadectomy on the development of tumors of the reproductive tract

Sparing effect of spaying on the development of mammary tumors - Mammary neoplasms are the most common tumors found in female dogs with estimates of a lifetime risk for developing malignant tumors ranging from 2% to more than 20%.^{18,19} In cats the incidence is less than half that of dogs. However, these tumors account for 17% of neoplasms in female cats,^{18,20-22} and at least 85% of feline mammary tumors are malignant.^{20,21,23} There is some evidence supporting a breed-associated predisposition: Siamese cats, Domestic shorthair cats, several Spaniel and Poodle breeds and the Dachshund seem to be predisposed. Apart from the genetic predisposition, gonadal hormones seem mainly to influence the pathogenesis of mammary tumors. Spayed dogs and cats are significantly less affected by mammary tumors than intact animals, but the timing of spaying also plays a critical role. The risk of developing malignant mammary tumours in dogs spayed prior to the first estrus is reduced by 99.5 % compared to intact dogs. Dogs spayed after the first and before the second estrus had a 92% reduction in the risk of malignant mammary tumor development compared to intact dogs. According to the study by Schneider, et al, the sparing effect of gonadectomy on the development of malignant mammary tumors is lost after females have cycled more than twice or are older than 2.5 years of age.²⁴ However, the risk for benign tumor development appears to be reduced by gonadectomy even at a later age.²⁵ Similar effects are seen in cats: Cats spayed prior to 6 months of age had a 91% reduction in the risk of malignant mammary tumor development compared to intact cats. Those spayed prior to 1 year of age had an 86% reduction in risk, those spayed between 12 and 24 months of age had an 11% risk reduction, but spaying after 24 months of age provided no benefit.²⁶

Gonadectomy and survival rate after mammary tumor removal - According to several studies, performing an OVE or OVH at the time of or after mammary tumor excision does not significantly affect the survival time.^{24,27-29} In a study performed by Sorenmo, et al suggest, that OVH may be an effective adjunct to tumor removal in dogs with mammary gland carcinoma and that the timing of the OVH plays a critical role in survival time.³⁰ Dogs spayed within 2 years of the development of their malignant tumors had a survival advantage comparable to intact dogs or those spayed more than 2 years prior to mammary tumor development and mastectomy.³⁰

Tumors of the genital tract - In general, tumors of the genital tract are rare in spayed dogs and cats. Most canine uterine, canine and feline vaginal and vulvar tumors are leiomyomas. Because the occurrence of leiomyomas is mainly reported in intact female dogs and cats³¹⁻³⁴ and these tumors were not seen in bitches ovariectomized before 2 years of age,³⁵ a hormonal influence is strongly suspected. Furthermore, OVH at the time of tumor removal may be beneficial. In a review no bitches undergoing concurrent OVH had recurrence of vaginal or vulvar neoplasia.³³

Prostate cancer - Prostate cancer (PC) is rare in dogs (less than 0.6% in necropsy studies)³⁶ and very rare in cats, but is almost always malignant.

Castration has been evaluated as a treatment in human cases. The traditional thought was that neutering reduces testosterone levels, which should in turn reduce the risk of prostate cancer. However, although PC begins as an androgen-dependent tumour, the beneficial effects of androgen deprivation are often temporary and the development of an essentially incurable therapy-resistant PC seems to be almost inevitable during later stages. In 1987, a study of Michigan State University showed that castration at any age had no sparing effect on the risk of developing PC in dogs.³⁷ Furthermore, eight cases of PC were described in cats: all but one had been castrated.³⁸⁻⁴²

Over the last 5 years, several studies in dogs have identified an increased risk of neutered dogs to develop PC (with an odds ratio of 8 : 0 for prostate TCC, 2 : 1 for prostate Adenocarcinoma, 3 : 9 for prostate carcinoma and 2 : 8 for all prostate tumours).⁴³⁻⁴⁵ Compared to intact dogs with PC, neutered dogs with PC were more likely to fall into an older age category.⁴⁵ Apart from the reproductive status, the breed also affects the risk of

developing prostate tumors. Risk varies with breed, suggesting that genetics play a role in the development of prostate tumours.⁴⁵ Neutered mix-breed dogs, Shetland sheepdogs, Scottish terriers, Beagles, English Springer Spaniels, German shorthaired pointers and West Highland white terriers had significantly higher odds than the background population of neutered dogs to have prostate cancer.⁴⁵

Effect of spaying on external genitalia

Gonadal hormones are responsible for the normal development of the external genitalia. The effect of gonadectomy, and especially the time of gonadectomy, on the size of the vulva was examined in 3 groups of bitches and female cats. In cats and dogs gonadectomized at 7 weeks or 7 months, the vulva was small and infantile compared to intact females.^{46,47} In these studies no clinical problems were evident. However in dogs, perivulvar dermatitis is thought to develop more commonly in obese bitches that have an infantile vulva. The incidence of recessed vulva, perivulvar dermatitis and vaginitis is higher in spayed than in intact dogs and the incidence may even be higher in females spayed as puppies.⁴⁸

Vaginitis may occur as so-called juvenile vaginitis or subsequent to vaginal atrophy following gonadectomy. Whether the spaying of bitches with juvenile vaginitis will cause chronic vaginitis persisting to adulthood or even lifelong is controversial. In a review of 37 dogs with juvenile vaginitis, 84 percent of the cases resolved with or without treatment.⁴⁹ Allowing bitches with juvenile vaginitis to go through an estrous cycle may hasten resolution. However, it is unknown what effect increasing age and maturation of the immune system will have on the resolution of juvenile vaginitis.

Effects of testicular removal on the genital tract

Apart from the permanent suppression of reproductive function, bilateral orchiectomy has a prophylactic and therapeutic effect on androgen dependent diseases, such as benign prostate hyperplasia (BPH), chronic prostatitis, perineal adenomas and perineal hernias. In fact 50% of intact dogs exhibit histological evidence of BPH by 5 years of age.⁵⁰ In addition, BPH predisposes dogs to prostatitis, thus for both conditions castration is a suitable treatment. Castration also prevents testicular and epididymal disorders such as neoplasia, torsion of the spermatic cord, orchitis and epididymitis. This is especially important in male dogs as the testicles are the second most common anatomical sites for cancer development.⁵¹ These diseases are very rare in tomcats.

Effects of the timing of testicular removal on the genital tract - Testosterone is responsible for the normal development of the penis and prepuce in dogs and cats and for the penile spines in tomcats. The effect of gonadectomy on the external genitalia was investigated in male cats and dogs neutered at 7 weeks, 7 months and compared with intact males.^{46,47} The most striking differences in the development of secondary sex characteristics were the immaturity of the prepuce, penis and os penis of male dogs neutered as puppies. The immature nature of the external genitalia reflects their dependency on androgens for normal growth. The slightly higher testosterone secretions in male dogs neutered at 7 months of age may have been enough to promote some growth of the prepuce, penis, and os penis, but not to the same extent as the sexually intact dogs. In cats, complete penile extrusion was possible in 100% of intact cats, 60% of cats neutered at 7 months and in no cat neutered at 7 weeks of age.⁴⁶

Effects of gonadectomy on the lower urinary tract

Urinary incontinence - The risk of urinary incontinence (UI) is low in intact bitches. The incidence of UI due to spaying varies between 3 and 21%, depending on the author.⁵²⁻⁶⁵ UI

after spaying can occur immediately or up to 10 years after surgery.⁵³ More than half of the bitches become incontinent in the first year and about 75% within 3 years after gonadectomy. In most cases the cause for UI after spaying is a reduction in the urethral closure pressure.⁶⁶

The risk for urinary incontinence is influenced by various factors such as body weight or breed and time of spaying. Dogs weighing less than 20 kg have a 10% risk of becoming incontinent after spaying, whereas in dogs weighing more than 20 kg, the risk is 30%.^{53,61} Boxers, dobermans, bobtails, giant schnauzers and rottweilers all have a known predisposition for UI. A study performed in 2005 in Germany and Switzerland showed that 71% of boxers spayed after the first heat became incontinent. Spaying shortly before puberty seems to reduce the risk by 50%.^{53,61,63} In another study, bitches were significantly more likely to develop UI when spayed at less than 3 months of age than bitches spayed between 3 months and one year of age.⁶⁷

The pathophysiology of urinary incontinence is still unclear. Altered GnRH, FSH and LH secretion after gonadectomy may be involved.^{61,68-73} In most cases, UI due to spaying is easily controlled with the treatment of alpha-adrenergic substances.^{74,75}

FLUTD - A recent survey of veterinary surgeons in practice, "When to neuter dogs and cats", found that the most common medical concern raised was the possibility of increased risk of FLUTD with early neutering.⁷⁶ Numerous studies have been performed to examine the effect of gonadectomy on urinary health in cats, most failing to detect a correlation between gonadectomy of cats at any age and an increase in incidence of FLUTD or other problems associated with this condition. Gonadectomy had no effect on urethral function in cats, as determined by urethral pressure profiles.⁷⁷ Furthermore, similar urethral diameters, as well as no difference in pre-prostatic and penile urethra, were found in cats neutered at 7 weeks, 7 months or those remaining intact.⁴⁶ A long-term study performed to compare effects of prepubertal and traditional-age gonadectomy found no increased risk of FLUTD in early-neutered cats up to 3 years after surgery.⁷⁸

However, in one large study of male and female cats, both gonadectomy and obesity were found to be risk factors for the development of FLUTD.⁷⁹

Transitional cell carcinoma - Transitional cell carcinoma (TCC) rarely occurs, however there is considerable variation in the risk of canine TCC. Epidemiological studies of TCC in dogs have revealed a number of risk factors, including breed, female gender, reproductive status, and obesity as well as environmental factors, such as insecticide exposure.⁸⁰ Scottish terriers have a 18-fold increased risk compared with mixed breeds. Females have a 2-fold increased risk compared to males, gonadectomy increases the risk more than 4 times in females than in male dogs.⁸⁰ The increased risk for developing TCC in neutered dogs of both sexes is not explained at this time.

Effect of gonadectomy on metabolism

Body weight - Although obesity can occur in both neutered and intact animals and is influenced by a number of factors such as diet, breed, and activity level, there are data indicating that neutered animals may gain significantly more weight compared to intact animals. While results of several studies indicate that neutering is a risk factor for obesity in cats (neutered cats are 3.4 times more likely to become obese than sexually intact cats),⁸¹⁻⁸³ there is conflicting information on whether dogs are more likely to experience weight gain after neutering. Information on 8,268 dogs was gathered from 11 veterinary practices in the UK. Spayed female dogs were about twice as likely to be obese as intact female dogs.⁸⁴ In female Beagle dogs, ovariectomy induced a significant decrease of daily energy requirement, and with ad libitum feeding the food consumption increased considerably and the dogs gained excess body weight.^{85,86} However, in a study of 44 adult working dogs similarly fed and worked, no change in body weight was found among sham-operated and ovariectomized bitches.⁸⁷ The time of gonadectomy is also controversially discussed: In a 15 months

prospective study performed to compare the effect of early and traditional age neutering of intact animals, no differences in food intake, weight gain or back-fat depth among neutered and intact animals were found.⁴⁷ However, the results of a recent population study indicate that neutering of dogs before 6 months of age is associated with lower prevalence of obesity compared to neutering after 6 months of age.⁶⁷ These results raise the question if early spaying reduces the increased risk of obesity after neutering in general?⁶⁷

Obesity is not necessarily a consequence of gonadectomy, but it is important to control the body weight in neutered animals. Obesity can be prevented by simple measures. There is evidence that cats on high dietary fat, but not carbohydrate, gain weight.⁸⁸ A low fat diet alone is however insufficient to prevent obesity after gonadectomy, as it requires the feeding of carefully controlled meals and not ad libitum.⁸² Prevention of obesity is important because of its association with increased risk of other medical problems⁷⁹ and the negative effects on the life expectancy.⁸⁹

Diabetes mellitus - Neutered cats are not only at a higher risk of becoming obese but have a 2 to 9 fold increased risk for developing diabetes mellitus than sexually intact cats.⁹⁰⁻⁹² The increased probability that cats will develop obesity and diabetes mellitus after gonadectomy may be due to decreased insulin sensitivity.^{81,93} A possible increase in the risk of developing diabetes mellitus was detected in castrated dogs. The possible association with obesity was not defined.⁹⁴

In intact bitches an altered glucose metabolism, induced by progesterone, occurs during pregnancy, metestrus and after progestin administration. Spaying is an integral part of the treatment of diabetes mellitus in these females.

Hypothyroidism - Two studies showed that neutering was the most significant gender-associated risk factor for the development of hypothyroidism.^{95,96} However in another study, using age matched controls and TSH response test results, neutering had no apparent effect on the likelihood of a dog being hypothyroid.^{97,98}

Effects of gonadectomy on the musculoskeletal system

Growth - The effect of gonadectomy on skeletal growth was already well known as eunuchoid growth in antique history. Studies examining the effects of gonadectomy and time of gonadectomy showed that growth rate is unaffected, but physeal closure is delayed by gonadectomy.^{46,47} This is most obvious in male cats: Male cats neutered at 7 weeks or 7 months have on average final radial lengths of 13% greater than intact males.⁴⁶ It is controversial if the altered growth rate after gonadectomy at 7 weeks or 7 months of age has an effect on soundness.

Fractures - In cats, spontaneous femoral capital physeal fractures have been suggested to be a result of delayed physeal closure related to early neutering. In retrospective studies, 39 cats with 47 fractures have been examined.⁹⁹⁻¹⁰¹ 4 risk factors for spontaneous femoral capital physeal fractures in cats older than one year were suggested: Gender and reproductive status, delayed physeal closure and abnormally high body weight. Obese neutered male cats may be predisposed to femoral capital physeal fractures, which in turn emphasizes the importance of controlled feeding in early neutered cats. Population studies provide no association between age at gonadectomy and incidence of fractures in either cats or dogs.^{67,102}

Hip dysplasia - There is a possible influence of gonadectomy on the development of hip dysplasia. Neutered Boxers, with a mean age of 3 years at neutering, were 1.5 times as likely to develop canine hip dysplasia as sexually intact dogs.¹⁰³ As was previously discussed in the section on physeal fractures, it is speculated that this increase in risk may be explained by the influence of body weight. However, body weight was not included in this analysis, and there is no data on the influence of the timing of gonadectomy.¹⁰³

In a recent population study the influence of age at gonadectomy on development of hip dysplasia was also examined. Puppies that underwent gonadectomy before 5.5 months of age

had a 6.7% incidence of hip dysplasia, while those between 5.5 months and 1 year of age had an incidence of 4.7%. The authors speculated that this increased incidence may have resulted from altered hip joint conformation secondary to increased bone length.⁶⁷ However, considering the lower rate of euthanasia among early-age gonadectomized dogs with hip dysplasia in comparison to those that underwent later gonadectomy the author suggested that early-age gonadectomy may be associated with a less severe form.⁶⁷

Cranial cruciate ligament rupture - Gonadectomy has an influence on the prevalence of cranial cruciate ligament rupture (CCLR). The prevalence of CCLR is most common in neutered males, followed by spayed females, while intact animals have only half of the risk.¹⁰⁴ - Osteosarcoma

Osteosarcoma is a rare but highly malignant tumour, occurring mainly in large dogs.^{105,106}

Risk factors, such as increasing age, body weight, body size and gonadectomy, were established.¹⁰⁶⁻¹⁰⁸ A study comparing 3062 purebred dogs with osteosarcoma and 3959 purebred dogs without osteosarcoma, revealed a two-fold increased risk of osteosarcoma among neutered dogs when compared to intact dogs.¹⁰⁶ As the data did not include the age at gonadectomy, this study could not evaluate bone sarcoma risk in terms of duration of gonadal hormone exposure.

To test the hypothesis that endogenous sex hormones significantly influence bone sarcomagenesis, a study of Rottweiler dogs, a breed known to be at high risk for bone sarcoma, was performed.¹⁰⁸ Bone sarcoma was diagnosed in 12.6% of dogs in this cohort overall, with neutered dogs having a two-fold increased risk. However, gonadectomized female and male dogs lived longer than sexually intact dogs. The longer life expectancy may contribute to a higher overall cancer incidence in neutered animals. A significant association between gonadal hormone exposure and risk of bone sarcoma was found.¹⁰⁸ In males castrated before 1 year of age (lowest gonadal exposure) the risk for bone sarcoma was almost four times greater than in sexually intact males. In females spayed before 1 year of age bone sarcoma incidence was more than three times greater than the rate in sexually intact females.¹⁰⁸ The risk factor of early gonadectomy was found to be independent of adult height or body weight.¹⁰⁸

Effects of gonadectomy on various conditions

Cardiac tumours have a overall incidence of 0.19% in dogs¹⁰⁹ and 0.0275% in cats. Cardiac tumours occurred with similar frequency in male and female dogs, but the relative risk of developing a heart tumor for spayed females was > 4 times that of intact females.¹⁰⁹ Castrated males had only a slightly greater risk (1.6 times) of developing a heart tumour than intact males. No data is provided on the age at gonadectomy. However because most dogs with cardiac tumor were older than 10 years and data on the age of the control population is missing, a possible effect of the increased life expectancy of neutered dogs compared to intact dogs on the incidence of tumours cannot be excluded.

Diseases that are transmitted by mating or copulation, such as Sticker Sarcoma or brucellosis, are rarely observed in neutered dogs. FeLV and FIV are transmitted by mating, as well as by other direct social contacts. It is well known that castration reduces the territorial area and behaviour,⁸ but these diseases can also be transmitted by using the same feeding places. The time of gonadectomy does not seem to have an effect on the incidence of these diseases.⁷⁸

Life expectancy - It is well documented that neutered animals live longer than intact animals^{89,110}. The increased life expectancy in gonadectomized animals may be due to the preventive effect on diseases of the reproductive tract and/or the reduced risk-associated behavior. However, the increased life expectancy may also reflect to some extent the enhanced care of neutered animals by their owners.

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