

Is there a future for surgical contraception in the dog?



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Abstract

Many scientific studies have focused on the potential detrimental effects of surgical castration. Some studies observed an increase in the risk of developing certain types of cancers in neutered animals, males and females. However, there often appears to have been a breed predisposition. There are contradictory data about neutering effect on lifespan, probably due to the fact that sterilized and intact dogs do not face similar risks in their daily life. Castration often reduces unwanted behaviors, but may increase certain types of aggression towards other dogs or even humans, depending on the age when neutered. Other potentially increased risks reported in castrated dogs and bitches are bone and joint problems, including predisposition to hip dysplasia in some breeds, urinary incontinence in bitches, development of a 'puppy coat' or even loss of cognitive functions. Vasectomy or hysterectomy without ovariectomy may be surgical alternatives, but the best approach is probably to refer to guidelines for a rational choice to satisfy owners and optimize dogs' health.

Keywords: Neuter, dogs, cancers, lifespan, behavior, bones, joints, cognitive functions, alternatives

Introduction

Findings of recent studies regarding potential side effects of surgical castration on health or behavior in males and females have placed European veterinarians in a dilemma. It has become difficult for them to give accurate advice to dog owners. Practitioners prefer to avoid harming and endangering the future health of animals. They are also aware that sterilization is important to prevent uncontrolled reproduction and control the risk of abandoned puppies or adoption by irresponsible owners. This short review is not intended to provide answers, but to raise questions about the future of surgical sterilization.

Gonadectomy and cancers

A review that analyzed data on the role of neutering in cancer development had inconclusive findings.¹ Bitch owners in France consider ovariectomy from the perspective of preventing mammary tumors. Common concern is, does early neutering, substantially reduce the risk of mammary tumors in the bitch? This belief is based on a study published in 1969 that has not since been repeated.² However, a meta-analysis of 13 selected reports in English language peer-reviewed journals, had to exclude 10 manuscripts because of their high bias.³ Of the 3 remaining, 1 study detected an association between neutering and a reduced risk of mammary tumors. There were no evidence of association in 2 studies. Authors concluded that the evidence that neutering reduces the risk of mammary neoplasia, and the evidence that age of neutering has an effect, are judged to be

weak and are not a sound basis for firm recommendations. Even if this belief appears to be probably true for most veterinary practitioners following bitches throughout their lives (as very few bitches spayed at an early age develop mammary tumors), it is not appropriate to present this as a fact.

Hemangiosarcomas are frequent cancers in the dog, especially in some breeds such as the golden retriever. Some studies⁴ have pointed out the susceptibility of this specific breed, especially in spayed bitches, but age may have a larger effect on cancer-related mortality than reproductive status. However, the risk of hemangiosarcomas in golden retrievers is 4 times greater in females ovariectomized after 1 year of age compared to intact females or females neutered earlier in life.⁵

Regarding lymphomas and lymphosarcomas, a retrospective study published in 2018 on 6,201 dogs⁶ suggested an increased risk for neutered animals to develop this disease, both in males (OR = 2.8; 95%CI) and females (OR = 4.4; 95%CI). However, breed and sex are also important factors, independent of whether the animals are sterilized or not.

Osteosarcomas are the third cause of mortality in golden retrievers and have even a higher prevalence in giant breeds (e.g. rottweilers). Neutered golden retrievers animals (male and female) had substantially higher risk for osteosarcoma.⁴ A study in rottweilers⁷ suggested an increased risk in gonadectomized

animals (3 times in females and 4 times in males) to develop osteosarcoma, specifically, if the animals are spayed before 1 year of age.

Although the prevalence of prostatic carcinomas is lower (0.6%) in the general population there is an increased risk in castrated male dogs.⁸ Some breeds (e.g. Bouvier des Flandres) appear to have more cancer in females than in males. According to some authors,⁹ castrated animals from both sexes may have an increased risk. Transitional cell carcinomas of the prostate are also more likely to occur in castrated males.¹⁰

Mast cell tumors are rare in the general canine population but some breeds are believed to be predisposed such as golden retrievers (incidence: 2.4%), boxers, Boston terriers, or labradors. In males, vizslas¹¹ was identified to have increased risk of cancer in castrated dogs after 1 year compared to dogs castrated earlier or in intact dogs. In females, there was an increased risk for cancer after ovariectomy.¹²

Reasons explaining potential predisposition to develop some types of cancers in gonadectomized animal is not clear. After removal of gonads, LH is continuously elevated at supraphysiologic concentrations.¹³ As there are LH receptors in many neoplastic tissues (e.g. lymphomas, hemangiosarcomas, mastocytomas, transitional cell carcinomas, and osteosarcomas), it may be assumed that LH receptor activation in these various tissues may have a detrimental role in castrated animals. However, this remains to be confirmed.

Gonadectomy and lifespan

Several studies in the US based on a large number of animals, males or females suggested that castrated animals live longer than intact ones. For example, 1 study¹⁴ based on 40,000 sterilized and intact domestic dogs reported that sterilization was strongly associated with an increased lifespan. Also, data presented in 2013, based on 2.2 M dogs had similar findings.¹⁵ Spayed dogs lived an average of 11.6 years, 23% longer than intact female dogs, whereas neutered dogs lived an average of 11.1 years, 18% longer than intact male dogs.¹⁵ However, there may be some bias in these comparisons, as intact animals, especially male dogs, may live a more 'at-risk' life, perhaps due to the lifestyle of the owners or the medical care of pets that may differ between castrated and intact dogs, or because the hormonal drive of dogs that may lead them to face more dangerous situations. For example, intact dogs are more than twice as likely to be hit by a car or bitten by another animal as neutered dogs. Sterilization decreased the risk of infections,¹⁴ perhaps due to the withdrawal of progesterone and testosterone, which have an immunosuppressive effect. Also, intact male dogs were more likely than sterilized dogs to roam and to fight with other dogs, and intact bitches may have more dominance aggression than spayed females. Such behaviors may increase the risks of infectious or traumatic, direct or indirect causes of death.

Some factors linked with castration are to be taken into account

when studying lifespan and gonadectomy. For example, median lifespan was shorter in overweight animals compared to normal weight dogs, with breed specificities.⁶ However, these differences were highest in Yorkshire terriers and least in German shepherd. According to these authors, it is important to promote healthy body condition in castrated animals.

More than 10 years data on rottweilers suggested that ovariectomy at a young age decreased the risk of mammary tumors.¹⁷ According to these authors, it is important to consider issues more broadly and not only in terms of risk for certain diseases, but in terms of the effect on the whole body. In contrast to what was believed and taught for decades ('ovariectomy is good for health'), several studies indicate that the presence of ovaries is part of an overall system that promotes longevity. Certainly, bitches that are not spayed have a higher risk of developing mammary tumors and pyometra. However, these authors studied whether bitches that developed mammary tumors or pyometra during their lifetime had a clearly shortened lifespan or not. Nearly 50% of mammary tumors in dogs are benign and also due to good medical care of pets in western countries (currently, diagnosis and surgical treatment of mammary tumors and pyometra are usually performed early). Therefore, the lifespan of the majority of affected bitches is not compromised. On a population level, mammary tumors or pyometra did not affect their longevity.¹⁷ In contrast, bitches < 4.3 years had increased ($p = 0.002$) longevity of 33% compared to females spayed early, an average increase in lifespan of 17 months. In fact, other diseases that are clearly more serious for longevity and linked to sterilization have to be considered: lymphomas and osteosarcomas in particular, not to mention other diseases (e.g. obesity and diabetes) directly or indirectly linked to hormonal changes following ovariectomy. In other words, ovario-hysterectomy performed in young bitches would substantially reduce life expectancy. Studies are to be continued in other breeds and on a larger number of animals before drawing firm conclusions.

Gonadectomy and behavior

Male dogs

It is important to differentiate between undesirable behaviors potentially linked to testosterone and behavioral disorders. Undesirable behaviors (urinary marking, roaming, mounting people's legs or inter-male aggression) are often considered by the owners as normal phenomenon. Two-thirds of dogs encountered at least 1 of 4 undesirable behaviors as per a survey (Virbac, unpublished data). Very often, owners are bothered by them (for example, 31% of the owners were bothered by inter-male aggression and 51% by urinary marking), but in the majority of cases (nearly 75%), they do not discuss it with their veterinarian or do not even consider mentioning, because they feel that these normal behaviors in male dogs for which nothing can be done to decrease the inconvenience it causes.

What is the effect of gonadectomy on these undesirable behavioral situations? Some studies considered this; for example, there were

modifications of behavior in 122 dogs after surgical castration.¹⁸ Urinary marking inside the house decreased by 69% and outside decreased by 23% but was not completely stopped. Roaming, when it was induced by bitches in estrus, decreased by 64%, but roaming due to other causes (e.g. hunting dogs) decreased only by 16%. Mounting on people's legs decreased by 57%, mounting on other males decreased by 43%, and mounting on bitches decreased by 41%.¹⁸ However, mounting inanimate objects (e.g. cushions) decreased only by 26% and was even increased by 5% in some. Regarding inter-male aggression, 23 dogs had this unwanted behavior, 13 dogs improved, but 1 dog even became more aggressive after castration. Most other studies had similar numbers with slight differences. For example, 48 of 35 (73%) did not have any modifications on urinary marking outside and only 9 dogs (19%) had a decreased frequency of urinary marking, and 4 dogs (8%) even began to sit down to urinate as prepubertal animals.¹⁹ We can therefore roughly estimate that, after castration, undesirable behaviors decrease, but are not completely eliminated in ~ 60% of cases.

The relative failure of gonadectomy toward inter-male dominance or other unwanted behaviors is not surprising. A study²⁰ conducted in free-roaming dogs in Chile reported that castrated dogs had no reduction in sexual activity or fighting behavior with other males. In other words, these undesirable behaviours are only partly linked to testosterone.

Furthermore, aggression towards humans was another problem that was addressed in most studies. After castration, aggression towards strangers decreased in 22%, but increased in 4% of animals.¹⁸ In the same study, aggression towards familiar people also increased by 4%. In other words, after castration, some male dogs may become more aggressive towards other dogs and also towards people. A retrospective study²¹ on 13,498 male dogs aggression to humans and 13,237 dogs aggression to other dogs used the C-BARQ scale (canine behavioral assessment & research questionnaire), a standardized, behavioral evaluation tool. It appeared that some dogs became more aggressive with strangers, especially if castrated between 7 and 12 months of age, a common practice in Europe. These authors therefore concluded that their data did not support the view that gonadectomy will predictably reduce aggressive behavior. Veterinarians need to consider these facts when counseling and informing owners about the advantages and disadvantages of castration in order to avoid potential owner complaints or even legal actions against the veterinarian if the dog bites someone (e.g. a child).

What about medical castration? In 2007, subcutaneous implants containing the GnRH super-agonist deslorelin (Suprelorin®, Virbac) was released on the European market. Surgically castrated male dogs and dogs implanted with Suprelorin® 4.7 mg were compared.²² Effects on mounting, urine marking, roaming and inter-male dominance were identical. In other words, when a veterinarian hesitates to surgically castrate a male with an undesirable behavior without knowing whether it will improve the dog's behavior or not, using an implant may be a good alternative to test the effect

of castration. If it works, then the dog may be surgically castrated later, being more confident about the success of the procedure.

Behavioural pathology is an even more complicated matter when we consider gonadectomy. Among 1,644 dogs, significantly more neutered male dogs were admitted to a teaching hospital for aggression and phobias compared to the percentage of neutered dogs admitted to other departments of the same hospital.²³ The authors concluded that 'these findings deserve attention from the veterinary community and suggest to reexamine the recommendations of gonadectomy for dogs'. In other words, gonadectomy may be useful in case of slightly unwanted behaviors, but may become contraindicated in case of real behavioral disorders. Among 2,505 castrated male dogs from the vizsla breed had 1.3 more risk to develop a behavioral disorder, and even more if castrated before 6 months of age (1.8 times more risk).¹¹ Therefore, if a dog is presented with a potential behavioral disorder, it is wise to seek advice from a behavioral specialist or at least to begin by a behavioral treatment before 'jumping' to have surgical gonadectomy. A Lakeland terrier that had anxiety separation was castrated by a veterinarian (owners were not told that castration could increase the problem).²⁴ After castration, it started to howl at night and the author felt that it would have been wise to postpone castration while waiting for the advice of a behaviorist.

The potential negative effect of gonadectomy on behavioral disorders is especially interesting to bear in mind, when we know that thousands of dogs are abandoned in Europe, many for unwanted behavior. Different behavioral disorders may be associated with an insufficient duration of exposure to gonadal hormones before castration.²⁵ The authors wrote that 'shelters are inundated by dogs displaying undesirable behaviours'. It remains to be known as to how many inappropriate castrations result in behavioral issues and subsequent abandonment.

Female dogs

This issue is not so clear in females, although some publications suggest a potential increase of aggressions in spayed bitches.^{26,27} Significantly higher 'dominance aggression' towards family members was observed more in spayed bitches.²⁸ In Labrador retrievers, owners of spayed bitches observed more frequent or more intense fear reaction in their animals in response to loud noises, unfamiliar objects approaching on or near the sidewalk, or if they were approached by unknown dogs barking, growling or jumping.²⁹ In contrast to popular belief, gonadectomy did not inevitably result in a behaviorally more stable dog.²⁹ As in male dogs, caution should be taken by veterinarians when owners are requesting ovariectomy in a bitch for behavioral disorders.

Other problems potentially linked with gonadectomy

Bone and joint problems

Among 1,170 intact German shepherd male dogs, 7% were diagnosed with at least 1 of 3 diseases (hip dysplasia, elbow dysplasia, and

cranial cruciate ligament rupture) and in neutered male dogs (neutered before 1 year of age), this incidence was significantly higher (21%).³⁰ Similarly, females spayed before 1 year of age had a significantly higher risk (17%) to develop at least 1 of these 3 orthopedic disorders compared to intact females (5%). In contrast, another study³¹ reported that neutering was not associated with these musculoskeletal diseases (including hip dysplasia).

Regarding hip dysplasia, in neutered male dogs of various breeds and sizes were significantly more likely to have clinical signs of hip dysplasia than dogs in the other study groups (intact males, intact females, and spayed females) (OR = 1.21; 95% CI = [1.18-1.24]).³² However, breed is another important risk factor to consider. In a study⁵ of 759 golden retrievers aged 1 - 8 years, the incidence of hip dysplasia in male dogs neutered before 12 months of age was twice that in the group of male dogs neutered after 12 months of age ((10.3 versus 5.1%, respectively, and significantly different).

In adult dogs, sex steroid hormones have major role in maintenance of bone tissue and its remodeling. They have an inhibitory effect on bone resorption, enabling a balance between resorption and osteosynthesis.³³ In women with bilateral ovariectomy, an increase in bone turnover and excessive bone resorption were observed.³³ However, regulation of this turnover can then be controlled by treatment with sex hormones. These same physiological hypotheses are put forward in dogs. In addition to their actions on bone tissue, these hormones are involved in other parts of the musculoskeletal system. In women, for example, it has been reported that estrogens act on joint cartilage, subchondral bone, muscles, ligaments and synovial membranes.³⁴

Concerning the potential increased risk of early spaying, it is now well known that castrating male or female dogs before puberty delays closure of growth cartilage in long bones (femur and humerus). The time of closure of the growth centers was significantly delayed in dogs neutered at 7 weeks of age, compared to those neutered at 7 months of age or older.³⁵ It may predispose to ligament problems (including hip dysplasia) or even epiphyseal fractures, in association with the weight gain and obesity often encountered after gonadectomy. Early neutering (before 5.5 months of age) was significantly associated with an increase in hip dysplasia (OR = 1.70; 95% CI = [1.04-2.78]).³⁶ Gonadectomized animals may be also predisposed to other ligamentary diseases such as rupture of the crucial ligament or elbow dysplasia. In labradors, the incidence of elbow dysplasia was significantly higher in dogs neutered at 6 months of age (4.2%) and between 2 and 8 years of age (2.2%) compared to the whole dog group (0.6%).³⁷

Urinary incontinence in bitches

The association between spaying and the subsequent development of urinary incontinence in bitches is well known, although not fully confirmed scientifically. There appears to be an increased risk of urinary incontinence after spay in certain large breeds, e.g. boxer, rottweiler, doberman, Irish setter, weimaraner, springer spaniel, bobtail, and giant schnauzer, whereas dogs of other breeds with a

similar body weight like the German shepherd and the labrador were rarely affected.³⁸ The surgical method of spaying, ovariectomy versus ovariohysterectomy, appears to have no effect on the risk for urinary incontinence, whereas the risk factor 'age at neutering' is still controversially discussed. The timing of gonadectomy relative to the onset of puberty may have an influence on the degree of incontinence. According to studies performed in Switzerland,³⁹ 60% of early spayed bitches had an uncontrolled loss of urine not only while sleeping but also when awake, during resting, and occasionally in a sitting position or on a walk. In contrast, bitches spayed after puberty are mainly incontinent during sleep, and even though more dogs spayed after the first estrus become incontinent, the frequency of incontinent episodes is considerably lower. A systematic review⁴⁰ of 7 selected peer-reviewed original English analytic journal articles that considered the effect of neutering or age at neutering on the risk of urinary incontinence concluded 4 articles to be at high risk of bias. Of the remaining 3 studies that were at moderate risk of bias, there was some weak evidence that neutering, particularly before 3 months of age, increases the risk of urinary incontinence. For these authors, the evidence overall was neither consistent nor strong enough to allow for strict recommendations on the effect of neutering or age at neutering on the risk of urinary incontinence.

Dematological problems

Certain breeds, such as the Irish setter, cocker spaniel, longhaired dachshund, eurasier, chow-chow, golden retriever, Newfoundland and landseer, longhaired Belgian shepherd, Afghan hound, etc, have a predisposition for coat changes after spaying. Affected dogs have substantial increase of wool hair and decrease in hair color intensity. The coat resembles that of young dogs and is called 'puppy coat'.⁴¹ These may be so severe that breeders advise against spaying. However, it is unknown to what extent reproductive hormones influence hair growth. From our own experience, this may happen in male dogs and in bitches after surgical gonadectomy. GnRH agonists subcutaneous implants may help to restore – at least partially – the initial quality of the coat.⁴¹

Loss of cognitive functions

Some authors hypothesize that cognitive decline in neutered senior dogs appears to progress more rapidly than in intact dogs.⁴² Their results suggest that the presence of circulating testosterone in aging sexually intact male dogs may slow the progression of cognitive impairment, at least among dogs that already have signs of mild impairment. Estrogens would be expected to have a similar protective role in sexually intact female dogs; unfortunately, too few sexually intact female dogs were available for inclusion in this study to test this hypothesis. Androgen deprivation results in decreased synaptic connections in the hippocampus of rodents and nonhuman primates, associated with an increased amyloid deposition in the brain.⁴³ However, another study⁴⁴ in beagles (10 years old) based on brain histological analyses, refuted this conclusion.

Other surgical approaches

Although most studies on surgical castration are focused on gonadectomy, there are other forms of desexing that enables a dog to keep their gonads intact while preventing reproduction.^{13,21,45} In male dogs, vasectomy is a surgical alternative method for desexing. This procedure consists of surgical transection of the vas deferens, leading to azoospermia and consequently, infertility, without apparently affecting testicular structures or testosterone concentrations.^{45,46} Even if vasectomy may be a suitable option for male contraception and useful in free-roaming and/or feral dogs as a potentially effective means of population control,⁴⁵ it has not been widely adopted in practice. It appears that it does not result in changes in libido nor other male-specific behaviors in dogs,⁴⁵ and specific complications appear to be rare and include spermatocele,⁴⁷ sperm granuloma,^{47,48} and testicular degeneration.⁴⁹ Nevertheless, there is a need to further explore the long-term consequences of vasectomy. In beagles, vasectomy led to irreversible damage to testes structure and other health problems.⁵⁰act on joint cartilage, subchondral bone, muscles, ligaments and synovial membranes.³⁴

In female dogs, other surgical approaches (other than ovariectomy and ovariectomy) are not widely used in practice. However, surgical transection of the uterine tubes (ovary-sparing hysterectomy) is more frequently performed.⁴⁵ Their medical consequences are not well studied and like vasectomy for male dogs, these alternative desexing methods do not change the hormonal status of the bitch.⁴⁵ Therefore, the expected various health consequences are similar to those in intact individuals, inasmuch as the susceptible organs remain in the body. More research is needed on the medical complications of these alternative surgical approaches.

How to make a rational choice, satisfy the owners and optimize the health of the dog

In small dog breeds, the occurrences of cancers and joint disorders were low or even close to zero in both intact and neutered dogs, with exceptions of Boston terrier and shih tzu, where there was a significant increase in cancers after neutering.⁵¹ These authors proposed and published interesting guidelines for the best age for neutering in 35 breeds, to avoid increasing long-term health risks of neutering. Same authors⁵² suggested the risks of 1 or more joint disorders following early neutering can be predicted on the basis of the dog's body weight. Those dogs that are expected to reach at least 20 kg as adults had a significantly increased risk of having 1 or more joint disorders, that is up to 20% above the level of intact dogs.

Conflict of interest

None to report.

References

1. Smith AN: The role of neutering in cancer development. *Vet Clin North Am Small Anim Pract* 2014;44:965-975.
2. Schneider R, Dorn CR, Taylor DO: Factors influencing canine mammary cancer development and postsurgical survival. *J Natl Cancer Inst* 1969;43:1249-1261.
3. Beauvais W, Cardwell JM, Brodbelt DC: the effect of neutering on the risk of mammary tumours in dogs-a systematic review. *J Small Anim Pract* 2012;53:314-322.
4. Kent MS, Burton JH, Dank G, et al: Association of cancer-related mortality, age and gonadectomy in golden retriever dogs at a veterinary academic center (1989-2016). *PLoS One*. 2018;13:1-12.
5. Torres de la Riva G, Hart BL, Farver TB, et al: Neutering dogs: effects on joint disorders and cancers in Golden Retrievers. *PLoS One*. 2013;8:1-7.
6. Bennett PF, Taylor R, Williamson P: Demographic risk factors for lymphoma in Australian dogs: 6201 cases. *J Vet Intern Med* 2018;32:2054-2060.
7. Cooley DM, Beranek BC, Schlitter DL, et al: Endogenous gonadal hormone exposure and bone sarcoma risk. *Cancer Epidemiol Biomarkers Prev* 2002;11:1434-1440.
8. Teske E, Naan EC, Van Dijk EM, et al: Canine prostate carcinoma: epidemiological evidence of an increased risk in castrated dogs. *Mol Cell Endocrinol* 2002;197:251-255.
9. Mutsaers AJ, Widmer WR, Knapp DW: Canine transitional cell carcinoma. *J Vet Intern Med* 2003;17:136-144.
10. Bryan JN, Keeler MR, Henry CJ, et al: A population study of neutering status as a risk factor for canine prostate cancer. *Prostate* 2007;67:1174-1181.
11. Zink MC, Farhooody P, Elser SE, et al: Evaluation of the risk and age of onset of cancer and behavioral disorders in gonadectomized Vizslas. *J Am Vet Med Assoc* 2014;244:309-319.
12. White CR, Hohenhaus AE, Kelsey J, et al: Cutaneous MCTs: association with spay/neuter status, breed, body size, and phylogenetic cluster. *J Am Anim. Hosp Assoc* 2011;47:210-216.
13. Kutzler MA. Possible Relationship between Long-Term Adverse Health Effects of Gonad-Removing Surgical Sterilization and Luteinizing Hormone in Dogs. *Animals* 2020;10:599:1-11.
14. Hoffman JM, Creevy KE, Promislow DE: Reproductive capability is associated with lifespan and cause of death in companion dogs. *PLoSOne* 2013;8:1-7.
15. <https://fr.scribd.com/document/140196171/Banfield-Pet-Hospital-State-of-Pet-Health-2013-Report>
16. Salt C, Morris PJ, Wilson D, et al. Association between life span and body condition in neutered client-owned dogs. *J Vet Intern Med* 2019;33:89-99.
17. Waters DJ, Kengeri SS, Maras AH, et al: Life course analysis of the impact of mammary cancer and pyometra on age-anchored life expectancy in female Rottweilers: Implications for envisioning ovary conservation as a strategy to promote healthy longevity in pet dogs. *Vet J* 2017;224:25-37.
18. Maarschalkerweerd RJ, Endenburg N, Kirpensteijn J, et al: Influence of orchietomy on canine behaviour. *Vet Rec* 1997;140:617-619.
19. Andersson A, Linde-Forsberg C: Castration and progestagen treatment of male dogs, part 2. *Eur J Companion Anim Pract* 2002;12:178-185.
20. Garde E, Pérez GE, Vanderstichel R, et al: Effects of surgical and chemical sterilization on the behavior of free-roaming male dogs in Puerto Natales, Chile. *Prev Vet Med* 2016;123:106-120.
21. Farhooody P, Mallawaarachchi I, Tarwater PM, et al: Aggression toward Familiar People, Strangers, and Conspecifics in Gonadectomized and Intact Dogs. *Front Vet Sci* 2018;5:18.

22. De Gier J and Vinke CM. Use of deslorelin to control hypersexuality in male dogs. Proc 7th EVSSAR congress 2010:9-11.
23. Bamberger M, Houpt KA. Signalment factors, comorbidity, and trends in behavior diagnoses in dogs: 1,644 cases (1991-2001). J Am Vet Med Assoc 2006;229:1591-1601.
24. What is your client thinking. Will neutering change his behaviour? Vet Rec 2019:70.
25. McGreevy PD, Wilson B, Starling MJ, et al: Behavioural risks in male dogs with minimal lifetime exposure to gonadal hormones may complicate population-control benefits of desexing. PLoS One. 2018;13:1-14.
26. Podberscek AL, Serpell JA: Aggressive behaviour in English cocker spaniels and the personality of their owners. Vet Rec 1997;14:73-76.
27. Reisner IR, Houpt KA, Shofer FS: National survey of owner-directed aggression in English Springer Spaniels. J Am Vet Med Assoc 2005;227:1594-1603.
28. O'Farrell V, Peachey E: Behavioural effects of ovario-hysterectomy on bitches. J Small Anim Pract 1990: 595-598.
29. Balogh O, Borruat N, Andrea Meier A, et al: The influence of spaying and its timing relative to the onset of puberty on urinary and general behaviour in Labrador Retrievers. Reprod Domest Anim 2018;53:1184-1190.
30. Hart BL, Hart LA, Thigpen AP, et al: Neutering of German Shepherd Dogs: associated joint disorders, cancers and urinary incontinence. Vet Med Sci 2016;2:191-199.
31. Howe LM, Slater MR, Boothe HW, et al: Long-term outcome of gonadectomy performed at an early age or traditional age in dogs. J Am Vet Med Assoc 2001;218:217-221.
32. Witsberger TH, Villamil JA, Schultz LG, et al: Prevalence of and risk factors for hip dysplasia and cranial cruciate ligament deficiency in dogs. J Am Vet Med Assoc 2008;232:1818-1824.
33. Almeida M, Laurent MR, Dubois V, et al: Estrogens and Androgens in Skeletal Physiology and Pathophysiology. Physiol Rev 2017;97:135-187.
34. Miyatake K, Muneta T, Ojima M, et al: Coordinate and synergistic effects of extensive treadmill exercise and ovariectomy on articular cartilage degeneration. BMC Musculoskelet Disord 2016;17:238 :1-11.
35. Salmeri K, Bloomberg M, Scruggs S, et al: Gonadectomy in immature dogs: effects on skeletal, physical and behavioral development. J Am Vet Med Assoc 1991;198:1193-1203.
36. Spain CV, Scarlett JM, Houpt KA: Long-term risks and benefits of early age gonadectomy in dogs. J Am Vet Med Assoc 2004;224:380-387.
37. Hart BL, Hart LA, Thigpen AP, et al: Long-term health effects of neutering dogs: comparison of Labrador Retrievers with Golden Retrievers. PLoS One 2014;9:1-10.
38. Arnold S, Arnold P, Hubler M, et al: Urinary incontinence in spayed female dogs: frequency and breed disposition. Schweizer Archiv für Tierheilkunde 1989;131:259-263.
39. Stöcklin-Gautschi NM, Hässig M, Reichler IM, et al: The relationship of urinary incontinence to early spaying in bitches. J Reprod Fertil (Suppl 57) 2001;57:233-236.
40. Beauvais W, Cardwell JM, Brodbelt DC: The effect of neutering on the risk of urinary incontinence in bitches - a systematic review. J Small Anim Pract 2012;53:198-204.
41. Reichler IM, Welle M, Eckrich C, et al: Spaying-induced coat changes: the role of gonadotropins, GnRH and GnRH treatment on the hair cycle of female dogs. Vet Dermatol 2008;19:77-87.
42. Hart BL: Effect of gonadectomy on subsequent development of age-related cognitive impairment in dogs. J Am Vet Med Assoc 2001;219:51-56.
43. Janowsky JS: The role of androgens in cognition and brain aging in men. Neuroscience 2006: 138;1015-1020.
44. Waters DJ, Shen S, Glickman LT: Life expectancy, antagonistic pleiotropy, and the testis of dogs and men. Prostate 2000;43:272-277.
45. Urfer SR, Kaerberlein M: Desexing dogs: A review of the current literature. Animals 2019;9:1086:1-28.
46. Whyte J, Sarrat R, Torres A, et al: Experimental vasectomy: comparison of the testicular structure with various surgical techniques. Actas Urol Esp 1998;22:178-183.
47. Pérez-Marín CC, Lopez R, Dominguez JM, et al: Clinical and pathological findings in testis, epididymis, deferens duct and prostate following vasectomy in a dog. Reprod Domest Anim 2006;41:169-174.
48. Mayenco Aguirre AM, Garcia Fernandez P, Sanchez Muela M: Sperm granuloma in the dog: Complication of vasectomy. J Small Anim Pract 1996;37:392-393.
49. Whyte J, Sarrat R, Torres A, et al: Effects of vasectomy on the testicular structure of the dog. Actas Urol Esp 1997;21:446-452.
50. Zhang Y, Wang X, Chen Z, et al: Long-term reproductive consequences of no-scalpel vasectomy in beagles. J Huazhong Univ Sci Technolog Med Sci 2012;32:899-905.
51. Hart BL, Hart LA, Thigpen AP, et al: Assisting decision-making on age of neutering for 35 breeds of dogs: associated joint disorders, cancers, and urinary incontinence. Front Vet Sci 2020;7:388:1-14.
52. Hart BL, Hart LA, Thigpen AP, et al: Assisting decision-making on age of neutering for mixed breed dogs of five weight categories: associated joint disorders and cancers. Front Vet Sci 2020;7:472 :1-12.