

Neutering in dogs and cats: current scientific evidence and importance of adequate nutritional management

Thiago H. A. Vendramini¹, Andressa R. Amaral², Vivian Pedrinelli², Rafael V. A. Zafalon¹, Roberta B. A. Rodrigues¹ and Marcio A. Brunetto¹* ©

¹Department of Animal Nutrition and Production of the School of Veterinary Medicine and Animal Science, University of São Paulo, Ave. Duque de Caxias Norte, 225, Pirassununga, SP, 13635-900, Brazil

²Department of Veterinary Internal Medicine of the School of Veterinary Medicine and Animal Science, University of São Paulo, Ave. Prof. Dr. Orlando Marques de Paiva, 87, São Paulo, SP, 05508-270, Brazil

Abstract

Neutering or spaying is a commonly recommended veterinary procedure. However, veterinarians are often confronted with conflicting findings and differences in concepts regarding practice and proper nutritional management after the procedure. The objective of the present review was to bring to light the most recent literature, summarise it and discuss the findings focusing on the risks and benefits of neutering in dogs and cats, and to determine the appropriate nutritional management for these animals.

Key words: Canine nutrition: Feline nutrition: Diet: Gonadectomy: Obesity

Introduction

One of the current major questions of veterinary practice is whether an animal should be neutered or not. Although apparently simple, the answer is highly complex, contradictory and may have implications not only for animal behaviour but also may present risk or even protective factors for disease development⁽¹⁻³⁾. On this matter, veterinarians are expected to be able to advise owners on castration and make sure that caring procedures, risks and benefits based on available research are easily comprehended.

Gonadectomy is often performed to promote health. According to Bailey⁽⁴⁾, several studies evaluated longevity and health in dogs and observed that neutered animals are more likely to suffer from reproductive diseases such as pyometra and non-cancerous prostate disease, breast and reproductive tumours, pregnancy-related disorders or unwanted hormoneassociated behaviour. On the other hand, numerous recent publications have identified specific complications related to gonadectomy in animals, with conflicting results between the studies, among which can be cited for example: neoplasic changes, surgical interventions, pyometra, behavioural/anxiety issues, prostate disease, urinary incontinence, obesity, dysplasia and ligament rupture⁽⁴⁾. According to Reichler⁽⁵⁾, this is mainly because gonadectomy confers a mix of benefits and adverse effects that depend on age of neutering, sex, species and breed⁽⁴⁾.

The development of recommendations for an informed case-by-case assessment requires an assessment of the risks and benefits of gonadectomy, including potential effects on neoplasia, orthopedic disease, reproductive disease, behaviour, longevity and population management, as well as anaesthetic and surgical risk complications. However, many factors other than neutered status play an important role in these outcomes, including breed, sex, genetics, lifestyle and body condition⁽⁶⁾.

The neutering procedure in dogs and cats is predominantly performed before puberty, between 7 and 10 months of age. Large and giant dog breeds tend to reach puberty later than smaller breeds; for this reason, large and giant breeds should be neutered or spayed at a later stage of life⁽²⁾.

Current prospects about the ideal age for the neutering of dogs and cats have been updated and published by Howe⁽⁷⁾, and it becomes clear that there is not a preferable age for this procedure. The decision of the ideal age for neutering is influenced by several factors, which include species, breed, sex, breed size and specific diseases of each breed, among others

There is a considerable disparity among veterinarians regarding recommendations given to pet owners, and thus the purpose of this review is to compile and present information in a clear and concise manner, addressing the indication of neutering, its possible risks, benefits, and the adequate nutritional management for neutered dogs and cats.

Abbreviations: CCLR, cranial cruciate ligament rupture; PLGH, percentage lifetime exposure to gonadal hormones.

* Corresponding author: Marcio A. Brunetto, email mabrunetto@usp.br



Population control

Dogs and cats are multiparous animals with short gestation time, with potential for producing numerous offspring that can reach sexual maturity at 6 months of age⁽⁸⁾. These factors associated with pet owners' lack of responsibility contribute to the abandonment and uncontrolled growth of the dog and cat population.

The main social pressure to perform a gonadectomy is a continuous overpopulation of unwanted dogs and cats and a perception that routine surgery reduces this population. Researchers found that intact animals were at greater risk of abandonment and unwanted descendants and threatened to represent an important factor affecting shelter animal populations⁽⁴⁾.

Castration thus becomes one of the most viable solutions in order to alleviate this problem and to prevent these animals from reproducing and consequently reduce the stray animal population. Gonadectomy performed before a dog reaches sexual maturity or adoption may address the issue of owner compliance, improve animal overpopulation and prevent the birth of unintended litters⁽⁶⁾.

According to the World Organization for Animal Health⁽⁹⁾, isolated activities of collection and euthanasia are not effective for population control. It is therefore recommended to act on the cause of the problem, which is mainly the lack of responsible care of pet owners and the uncontrolled reproduction of pets. The humanitarian method of population control consists of an extensive programme of neutering stray and client-owned animals, for those who do not wish to shelter any other pets or want to simply prevent their animals from breeding; and in conducting education campaigns for responsible care⁽⁹⁾.

There are differences in gonadectomy rates across the world, and these can be explained by differences in cultural differences and attitudes toward castration, and differences in economic status in rural and urban settings^(10,11). Improving veterinary training in paediatric anaesthetic and early gonadectomy techniques is mandatory for dog and cat gonadectomy before adoption, and further education of dog and cat owners about the reproductive physiology of small animals can only be beneficial in addressing these social issues⁽²⁾.

Risks and benefits for health

Neoplasia

A common justification for early spaying of bitches is the prevention of mammary gland neoplasia. However, references in the literature date from at least 50 years ago^(12–14), and this evidence has not been verified with the benefit of developing diagnostic methods and knowledge of potential biases such as age and breed.

A systematic review⁽¹⁵⁾ about the actual effect of spaying on the risk of developing mammary tumours in dogs, which involved screening more than 10 000 articles, has shown that there is some evidence suggesting that spaying before 2.5 years is associated with considerable reduction in the risk of malignant mammary gland tumours and this risk can be further reduced when spaying is performed before the first oestrus.

Another study has also described that mammary neoplasia is among the most common tumours observed in non-spayed bitches and about 50 % of these neoplasias are malignant⁽¹⁶⁾ and there are differences in the risk for development and malignancy among different dog breed sizes^(7,17).

Older studies showed that characteristics such as abnormal oestrus cycle, false pregnancy, pregnancy, litter numbers and offspring size do not represent major factors for increased risk of tumours^(18,19). However, the role of oestrogen in the aetiology of breast cancer in women is well established⁽²⁰⁾. The risk of developing breast cancer is believed to be influenced by total cumulative exposure of the breast tissue to bioavailable oestrogens and associated cumulative mitotic activity^(21,22), and the factors determining oestrogen exposure include early menarche, late menopause, nulliparity, pregnancy, obesity and use of oestrogen replacement therapy^(23,24).

Questionnaires completed by owners and veterinarians were used to obtain life-long medical and health information of 242 female Rottweilers, mainly assessing breast cancer and pyometra; although the risk of developing both diseases was positively correlated with ovarian hormone exposure, increased ovarian hormone exposure (≥ 4.3 years) was also associated with an overall longevity increase (a 33 % reduction in mortality, living 17 months longer than females with shorter ovarian hormone exposure)(25). According to the same authors, these findings cast doubt on the argument that elective ovariohysterectomy should be defended as an intervention that promotes longevity, based on protection against diseases that have a moderate risk of late mortality (breast carcinoma) or a low risk of mortality (pyometra)⁽²⁵⁾. However, it is important to note that the study was conducted only with Rottweiler females and, therefore, a genetic predisposition may play an important role.

Mammary gland tumours are also common in non-neutered cats, but the risk of development of this type of tumour in felines is about 50 % of that observed in $dogs^{(26)}$. However, 85 to 93 % of these tumours in cats are malignant and over 80 % of cats with malignant tumours already present metastasis at the moment of diagnosis⁽⁷⁾.

Spaying cats under the age of 1 year was associated with an 86% reduction in the risk of developing mammary gland neoplasia compared with non-spayed females^(27,28). Therefore, as in dogs, spaying in cats is extremely beneficial for the prevention of mammary neoplasia.

In male dogs, neutering can avoid testicular neoplasia⁽⁷⁾. Although it has been estimated that less than 1 % of intact male dogs die of testicular cancer⁽²⁹⁾, this low mortality rate is due to the high cure rate associated with the low risk of developing this type of tumour. Similarly, male cats rarely develop testicular neoplasia⁽³⁰⁾.

In general, genital tract tumours are rare in castrated dogs and cats. Most canine and feline uterine and vaginal tumours are leiomyomas. Because the occurrence of leiomyomas is mainly reported in intact bitches and queens^(31–34) and these tumours were not seen in ovariectomised female dogs before 2 years of age⁽³⁵⁾, hormonal influence is strongly suspected.

Vaginal and vulvar tumours account for 2-4 to 3 % of all dog tumours^(33,35,36). Leiomyomas are the most common vaginal tumours in dogs^(5,36,37). Because they occur most commonly in intact bitches, it is suggested that vaginal leiomyomas may be hormone-dependent^(36,37). Although this association has



not been proven, castration can have a substantial sparing

Teske et al. (38) investigated the frequency of prostate carcinoma in dogs and concluded that neutering influences the incidence of this disease. The procedure is not related to the onset of development but, instead, it favours tumour progression⁽³⁹⁾. However, similar to testicular neoplasia, the risk of a prostate tumour is extremely low (0.6 %) in companion animals⁽⁴⁰⁾.

In relation to other types of tumours, such as lymphoma, recently Bennett et al. (41) identified and quantified host risk factors for lymphoma in a large population of Australian dogs (n 6201). Neutered animals presented higher risk compared with intact animals in both male and female groups.

With the removal of the gonads, diseases such as ovarian tumours and cysts no longer occur. In addition, neutered dogs and cats are no longer susceptible to ovarian hormone-mediated disorders such as vaginal hyperplasia or uterine disease⁽⁵⁾.

However, the incidence of receding vulva, perivulvar dermatitis and vaginitis are higher in castrated than in intact bitches and the incidence may even be higher in neutered females when young(42). Finally, the incidence of urinary incontinence due to castration ranges from 3 to 21 % in different studies. In most cases, the cause of urinary incontinence after castration is a reduction in urethral closure pressure⁽⁴³⁾. The risk of urinary incontinence is influenced by several factors such as body weight, breed and age of castration⁽⁵⁾.

Other research conducted with veterinary surgeons found that the most common medical concern was the increased risk of lower urinary tract disease in neutered felines⁽⁴⁴⁾. In a large study of male and female cats, gonadectomy and obesity were risk factors for the development of feline lower urinary tract disease⁽⁴⁵⁾, but other previous studies showed no difference^(46,47). Therefore, further research on the subject is needed.

In enzootic areas where reproduction is poorly controlled and there is a large number of sexually active dogs roaming free, venereal tumours are the most common tumours in dogs^(48–50). Transmissible venereal tumours usually remain located in the external genitalia (48-50) and may become locally invasive. Metastases occur in up to 5 to 17 % of affected dogs (49,50). A decrease in mating behaviour would greatly reduce the transmission of venereal tumours(6).

Even cardiac tumours have been evaluated in castrated animals, and, despite the similar frequency in male and female dogs, the relative risk of developing a cardiac tumour in castrated females was four times that of intact females (51). However, as most dogs with heart tumours were older than 10 years and the age data of the control population are missing, it is not possible to exclude a possible effect of extended life expectancy of neutered dogs⁽⁵⁾.

Neutered animals may show increased rates of specific tumours, with the exception of mammary gland tumours. However, for almost all studies available in the literature, the relationship between neutering status and disease-specific risk may have been influenced by the age of animals used. In other words, if neutering increases life expectancy, neutered animals may present higher occurrences of end-of-life diseases (such as cancer) simply due to increased longevity. Hoffman et al. (52) compared the causes of death of more than 40 000 intact and neutered dogs and observed that neutering was associated with increased longevity, and although it reduced the risk of death from some diseases, such as infections, it increased the risk of death from others such as cancer. Thus, it should be considered that the probability of neutering as well as the likelihood of tumours increase with increasing age, so it is expected that animals that die from infectious diseases are more likely to be puppies and that animals who die of cancer are most probably older, so the exposure time of the gonads must be taken into consideration.

Still on this subject, a recently published study evaluated the association between mortality, gonadectomy and the development of cancer in golden retrievers⁽⁵³⁾. Whether the animal was castrated or intact, the risk of cancer-related death did not increase, but longevity did. The likelihood of being neutered increases with age; furthermore, the impact of the owner may play a role. Owner's awareness might be reflected in part by the reproductive status. Following this discussion in different breeds, Hart et al. (54) evaluated, over a period of 14.5 years, 1170 intact and castrated German shepherd dogs for joint disorders and cancer previously associated with sterilisation. Breast cancer was diagnosed in 4 % of intact females compared with less than 1 % in castrated females before 1 year. The occurrence of other types of cancer at 8 years of age was not higher in neutered dogs than in intact dogs⁽⁵⁴⁾. Furthermore, while investigating associations between age at gonadectomy and estimated risk or age at diagnosis of neoplasic disorders in Vizslas, Zink et al. (55) observed that gonadectomised dogs aged \leq 6 months, between 7 and 12 months or > 12 months old had significantly increased chances of developing cancer (i.e. mastocytoma and lymphoma) compared with the chances of sexually intact dogs. Gonadectomised females of ≤ 12 months of age and gonadectomised males and females of > 12 months of age had significantly increased chances of developing hemangiosarcoma compared with the chances of sexually intact dogs⁽⁵⁵⁾. Additional studies are necessary to verify the biological effects of gonadal hormone removal and the individuality and characteristics of each breed.

Immune system

A promising area of research that has not been explored in great depth is the impact of castration on the immune system and its ability to fight disease, as the reproductive and immune systems are highly interdependent⁽⁵⁶⁾.

Immune organs and tissues, such as thymus, lymph nodes and spleen, have receptors for steroid hormones⁽⁵⁷⁾. Earlier studies have shown that thymus ablation (the organ in which T lymphocytes mature) disrupted gonadal development and reduced steroid production⁽⁵⁸⁾; correspondingly, neutered male rats at an early age presented delayed thymic involution, thymic hyperplasia and decreased immune function⁽⁵⁹⁾.

In order to assess the relationship between the immune system and neutering, a recent study with dogs investigated the possible association between neutering and diseases associated with immune function compromise. The authors concluded that diseases such as hypoadrenocorticism, autoimmune haemolytic anaemia, atopic dermatitis, hypothyroidism, inflammatory bowel disease and thrombocytopenia present increased



prevalence in neutered dogs; that is, castration may result in a detrimental effect on the immune functions and health of companion animals⁽⁵⁶⁾. However, increased prevalence may be associated with other factors associated with castration, such as obesity.

The incidence of vaccine-associated adverse events has also been reported in the literature^(60,61) and the overall risk was higher for neutered v. sexually intact cats, according to the authors. One reason for these results is reduced oestrogen and testosterone, each acting in the physiological balance of protective immunity. Although oestrogens improve the humoral response, they inhibit cytokine release in human mast cells⁽⁶²⁾. Testosterone and its metabolites preserve the number of CD4⁺ and CD25⁺ regulatory T cells, which suppresses autoimmunity⁽⁶³⁾. The total immune impact of changes in sex hormones is yet to be elucidated, as the immunomodulatory effects of oestrogen and androgens on B-cell functions may also be indirectly mediated by gonadotropin-releasing hormone⁽⁶⁴⁾.

Skeletal system

Skeletal development is regulated by gonadal hormones that signalise closure of long bone epiphyseal plates. Thus, neutering before the closure of the epiphyseal plate may result in the overgrowth of these long bones⁽⁶⁵⁾, and contribute to a higher prevalence of joint disorders^(2,66–68).

Furthermore, studies have also suggested that neutering may influence the risk of cranial cruciate ligament rupture (CCLR) in pets. The CCLR in dogs is equivalent to humans rupturing their anterior cruciate ligament, a knee ligament. CCLR in dogs may occur due to trauma, but may also have genetic risk factors because some breeds appear to be predisposed, including the Labrador retriever. The definitive cause of CCLR has not been determined, but it probably has many factors⁽⁶⁹⁾.

In particular, two recent studies specifically investigated this issue and observed increased risk of injury independent of other factors (i.e. obesity) $^{(67,68)}$. Another recent study also showed that CCLR cases were more common in sterilised female dogs 1 year old or younger compared with sterilised female dogs older than 1 year old. For males, this finding was suggestive but not statistically significant, concluding that early sterilisation (≤ 1 year) may increase the risk of developing CCLR later in the life of Labradors (particularly in bitches) $^{(69)}$.

Evaluating different breed specifics, Hart *et al.*⁽⁵⁴⁾ observed that both intact male and neutered German shepherds were significantly more diagnosed with one or more joint disorders. The increased incidence of joint disorders primarily associated with early castration was the rupture of the cranial cruciate ligament⁽⁵⁴⁾.

Another widespread question regarding skeletal development is the relationship between neutering and hip dysplasia, and according to Hart *et al.*⁽⁶⁸⁾, the risk of development of this disease is higher in neutered dogs when compared with intact ones.

Obesity is also an important factor that may contribute to the development of cranial cruciate ligament injuries and hip dysplasia, and it is well documented that after neutering animals tend to gain excessive weight if food intake is not managed accordingly. Thus, these studies demonstrate the importance of body condition score control, especially for neutered pets.

Accordingly, there are concerns expressed by some veterinarians and owners about the increasing risk of spinal fractures in neutered adult male cats and its possible association with gonadectomy. Some studies have evaluated this (70,71), and increased body condition score was the main risk factor for fractures, not neutering.

Animal behaviour

Another important subject approached in order to favour the neutering of dogs and cats is its influence on behaviour. Sexually dimorphic behaviours are the most commonly exhibited by a sex, with mounting and spraying of urine as prime examples⁽⁷²⁾. Aggression can be a sexually dimorphic behaviour. More commonly, only forms of aggression associated with the presence of females in oestrus (aggression between females or between males housed with these females) are considered sexually dimorphic⁽²⁾. Gonadectomy and the subsequent decrease in gonadal steroid hormones were correlated with a decrease in sexually dimorphic behaviours^(46,73–77). Non-sexually dimorphic behaviours are not typically affected by gonadectomy⁽²⁾.

Duffy *et al.*⁽⁷⁸⁾ investigated canine aggression, and, against popular belief, results of the research suggest that neutered animals were more inclined to excessive aggressive behaviour instead of a gentler one. However, these behaviour effects appeared to be more specific for some breeds.

Another study assessing whether aggressive behaviour towards family members, strangers or other dogs was significantly different in gonadectomised dogs at various ages v. intact dogs was recently performed, and neither gonadectomy nor age of gonadectomy was associated with aggression against individuals or dogs. However, there was a small but significant increase in the chances of moderate or severe aggression against strangers in all gonadectomised dogs compared with intact dogs, but this effect was entirely driven by data from gonadectomised dogs at 7–12 months of age, who were 26 % more likely to show aggression to strangers. The authors concluded that given the growing evidence of significant adverse effects of gonadectomy to health, it is urgent to systematically examine other ways to prevent unwanted breeding, such as vasectomy and hysterectomy $^{(79)}$.

Recently Scandurra *et al.*⁽⁸⁰⁾ evaluated the effect of ovariectomy on the ability of females to follow human signals. A group of forty client-owned bitches (eighteen intact females and twenty-two gonadectomised females) were tested in the object selection task using the human proximal pointing gesture, and the results show a detrimental effect of ovariectomy on dogs' socio-cognitive skills related to responsiveness to pointing human gestures.

Regarding the period of gonadectomy and its effects on animal behaviour, Valcke⁽⁸¹⁾ assessed whether there is a difference in long-term undesirable behaviour between prepubertal gonadectomised cats and traditional-age gonadectomised cats. The conclusion of the research was that there is no detectable difference in the total number of potentially undesirable behaviours between groups, and that the evolution of these behaviours over 5–7 years is the same between the two groups.



According to Kustritz⁽²⁾, androgen deprivation has been associated with increased amyloid deposition in the brain of humans and rodents and decreased synapses in the brain of rodents and non-human primates⁽⁸²⁾. However, in a study⁽⁸³⁾ in which researchers directly examined brain tissue for DNA damage, a significantly higher percentage of neurons had extensive DNA damage in sexually intact Beagles than in castrated Beagles between 9 and 10.5 years old.

In addition, studies with rats have shown that neutering after adulthood impairs spatial memory (identification of objects and location)(84,85) and exogenous replacement of testosterone may re-establish these alterations (86,87).

Investigation of spatial abilities was also conducted. A recent study in dogs evaluated the effects of sex and gonadectomy on the spatial performance of dogs(88). This study provides the first evidence of an effect of ovariectomy on dogs' spatial cognition, in which intact females outperformed ovariectomised females in terms of learning speed and accuracy in learning task and memory.

Cats also exhibit behavioural changes associated with neutering, but, unlike dogs, reduced fights and decreased sexual behaviour (walking around for mating) in male cats are observed after the procedure, which is also correlated with a decrease in energy expenditure and weight gain⁽⁷⁷⁾.

A more recent study observed that neutering in cats before 5.5 months is actually associated with decreased sexual behaviour and territorial marking through urination, in addition to decreased aggression⁽⁸⁹⁾. However, for the prevention of behavioural changes before 1 year of life, attention should be directed to canine and feline sociability and not just on neutering⁽⁷⁸⁾.

Another study with dogs focused on the reported behaviour of 6235 castrated male dogs and calculated their percentage lifetime exposure to gonadal hormones (PLGH)(90). A total of forty behaviours differed between whole and neutered dogs, twentyfive of which were associated with PLGH and fourteen with the age of castration. Only two behaviours, urine marking and howling when left alone, were significantly more likely in dogs with longer PLGH. On the other hand, longer PLGH was associated with significantly reduced reporting of twenty-six behaviours, most of them undesirable. Of these, eight were related to fear and seven to aggression. These results suggest that the tendency of dogs to exhibit numerous behaviours may be influenced by the age at neutering, and indicate how the dog's behaviour matures when gonadal hormones are allowed to take effect⁽⁹⁰⁾.

Regarding anaesthetic and surgical complications, the present literature review reveals that there is a minimal difference in risk of surgical complications or subsequent developmental abnormalities between paediatric gonadectomy performed on dogs between 6 and 14 weeks of age and gonadectomy performed on 6-month-old dogs, both before puberty⁽⁶⁾. Studies^(2,91,92) regarding neutering by veterinary students found complication rates of 20 to 30 %, but the most common complications were considered minor problems and the occurrence rate was influenced by the experience of the individual performing the surgery. Thus, complications can be minimised by appropriate patient selection, use of safe and efficient anaesthesia protocols, application of minimally traumatic surgical preparation and surgical techniques, careful patient monitoring, and multimodal pain management, including preoperative analgesia (93,94).

Risk of post-neutering obesity

Neutering has been associated with weight gain and obesity. In a recent review of the effects of diet and gonadal steroids on appetite regulation and pet food intake, de Godoy⁽⁹⁵⁾ mentions that, overall, studies have revealed that gonadectomy is characterised by increased food intake and body weight, accompanied by physiological and behavioural changes. The papers listed in the review showed that different sex hormones affected eating differently. Androgens (i.e. testosterone) are anabolic hormones, resulting in increased food intake and lean tissue mass, while oestrogens are catabolic, decreasing food intake and body weight. Some studies have also shown associations between gonadectomy and changes in appetite-related hormones (i.e. ghrelin, leptin, adiponectin and glucagon-like peptide-1). However, the same author mentions that, overall, most scientific evidence to date has produced conflicting results, especially related to the effect of sex hormones and dietary interventions on appetite-related hormones and blood metabolites (95).

Fettman et al. (96) observed increased body weight and deposition of adipose tissue in castrated males and females compared with intact cats. Food intake also increased 3 months after the procedure in neutered animals, with no differences in nutrient digestibility. Furthermore, other studies have shown that energy intake increased after castration^(97,98).

However, considerations should be made regarding the interpretation and discussion of these results. For example, in the study by Houpt et al. (97), spayed bitches were fed ad libitum and perhaps, as a consequence, they presented higher food intake and weight gain, similar to the study of Fettman et al. (96)

A study performed by Jeusette et al. (98) has also evaluated the effect of gonadectomy, and the authors observed lower ad libitum energy intake in non-spayed bitches during oestrus, indicating that the effect is mainly related to the cyclical effect of oestradiol, in modulation of the satiating and orexigenic effect of intestinal hormones⁽⁹⁹⁾.

Kanchuk et al. (100) have also observed weight gain after neutering as a result of increased ad libitum energy intake and decreased energy expenditure. Insulin and leptin are considered signs of adiposity of the peripheral system that indicate the status of body energy reserves to the central nervous system; since the secretion and biological effect of these hormones are modified by gonadal mediators⁽¹⁰¹⁾, neutering may result in decreased expenditure and increased consumption of energy. The increase in food intake takes place fast, beginning 3 d after gonadectomy, and this acute effect is a result of the withdrawal of gonadal hormones, although it is unclear how plasma concentrations of these hormones have an influence over this matter.

In another study, Allaway et al. (102) aimed to determine the total energy requirement of kittens (15 to 52 weeks) by investigating the impact of castration and age on ingestion and body weight. Kittens were neutered when they were 19 or 31 weeks old and the results suggest that sterilisation in the early stages of sexual development may reduce the likelihood of acute changes in eating behaviour. From the standpoint of weight control and wellbeing, sterilisation before or at 26 weeks may be beneficial⁽¹⁰²⁾.





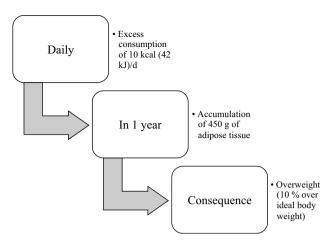


Fig. 1. Energy imbalance of neutered animals (adapted from Michel⁽¹⁰⁴⁾).

In order to add more information to the topic of satiety after neutering, a recent study (103) aimed to evaluate the effect of neutering on food intake, and especially blood concentrations of hormones related to satiety (blood ghrelin (active), cholecystokinin, total peptide YY and insulin) and activity of dogs. Neutering was not associated with inefficient control of food intake or variation in satiety hormones released in the gut, but was associated with decreased activity compared with intact dogs.

Based on current scientific literature, it can be assumed that the increased risk of obesity after neutering is not only motivated by increased energy intake but mainly by decreased energy demand and decreased activity (103). Obesity is mainly related to positive energy balance, in which energy intake is higher than energy expenditure, leading to its accumulation in the form of adipose tissue. This is illustrated in Fig. 1, adapted from Michel (104), in which a cat that consumes only 10 kcal (42 kJ) above its daily energetic requirements will accumulate, at the end of 1 year, about 450 g of adipose tissue. Depending on the size and breed of this cat, this may be equivalent to 10 % of its ideal weight, which means significant weight gain.

Thus, castrated cats have a higher risk of becoming obese, and therefore have a two to nine times greater risk of developing diabetes mellitus than sexually intact cats⁽¹⁰⁵⁻¹⁰⁷⁾. The increased likelihood of cats developing obesity and diabetes mellitus after neutering may be due to decreased insulin sensitivity(108,109). In intact bitches, altered progesterone-induced glucose metabolism occurs during pregnancy, metoestrus and after progesterone administration. Neutering is an integral part of the treatment of diabetes mellitus in these cases⁽⁵⁾.

According to Le Roux⁽¹¹⁰⁾, BMR is also directly related to weight gain after neutering. This author evaluated ovariectomised bitches fed with a pre-determined amount of complete commercial food, and after spaying a decrease in BMR and a tendency for energy expenditure reduction were observed.

Thus, in order to stimulate maintenance of ideal body weight, exercise, provision of an adequate amount of food and constant body condition score monitoring are necessary for proper management of neutered animals.

Nutritional management after neutering

Hormonal status and reduction of physical activity are two important factors that affect energy expenditure, leading to a decrease in energy demand and, consequently, the need to adjust nutritional management after neutering(111-113).

Feeding ad libitum should be avoided and any amount of food supplied should be in accordance with the energy requirement estimated with specific equations.

The National Research Council (114) recommends the use of the equation 130 kcal (544 kJ) \times (kg body weight)^{0.75} for daily energy requirement calculation for active dogs. However, for neutered animals, due to the decreased energy demand, the equation for inactive dogs is usually necessary, and corresponds to 95 kcal (397 kJ) × (kg body weight)^{0.75} or even less, depending on an individual evaluation of the patient (114,115).

Regarding the maintenance energy requirement for cats, a specific equation for neutered animals should be applied based on information from the European Pet Food Industry Federation (FEDIAF)⁽¹¹⁵⁾, which recommends per d 75 kcal (314 kJ) x (kg body weight)^{0.67}. As for active cats, daily energy requirement should be estimated according to equation of 100 kcal (418 kJ) x $(kg body weight)^{0.67}$.

In order to exemplify and illustrate the lower energy requirement after neutering, Fig. 2 and Fig. 3 illustrate the examples of a dog with 10 kg body weight and a cat with 3 kg body weight, in which the equations of the National Research Council (114) and FEDIAF⁽¹¹⁵⁾ are applied, before and after neutering.

Risk factors associated with the occurrence of overweight and obesity are mainly related to the owner's lack of perception regarding true body condition of the animal, considering it normal when it is overweight (116). Thus, one of the key points for appropriate nutritional management after the procedure is assessment of body condition score(117). The correct evaluation of body condition score in all animals helps to identify and avoid weight gain in the early stages; however, for ideal assessment the evaluators must be trained and have experience with the technique.

Energy density is one of the main different characteristics of a diet specifically formulated for neutered animals, with low energy density being of major importance for this matter. A recent study conducted by Spofford et al. (118) evaluated a diet with low energy and fat content and observed that dietary energy is positively correlated with weight gain after neutering in cats. Lund et al. (119) have also demonstrated that uncontrolled food intake contributes to weight gain in neutered male cats due to its higher energy density.

A study by Schauf et al. (103) has also evaluated the effect of feeding high-carbohydrate or high-fat diets on consumption and on satiety factors of dogs before and after neutering. The authors concluded that the intake of a high-carbohydrate diet tends to increase the concentrations of mediators involved in satiety regulation (cholecystokinin and total peptide YY). Similarly, Backus et al. (120) observed that replacing carbohydrates with fat does not seem to prevent weight gain in neutered cats. There is also scientific evidence that diets with high fibre and protein content improve satiety in companion animals⁽¹²¹⁾. In addition, as glycaemia and insulinaemia are directly related to





Species: canine/BCS: 5/MMS: 3

Body weight: 10 kg

Food metabolisable energy: 4.04 kcal/g

Before neutering After neutering MER for maintenance of active dogs MER for maintenance of inactive dogs $130 \times (body weight)^{0.75} = kcal/d$ $95 \times (bodv weight)^{0.75} = kcal/d$ $130 \times (10)^{0.75} = \text{kcal/d}$ $95 \times (10)^{0.75} = \text{kcal/d}$ 731.04 kcal/d 534.22 kcal/d Amount of food to be provided Amount of food to be provided MER/food metabolisable energy MER/food metabolisable energy 731 · 04 kcal/d/4 · 04 kcal/g 534·22 kcal/d/4·04 kcal/g 180·95 g/d 132·23 g/d Reduction of 27 %

Fig. 2. Effect of neutering on energy requirement for adult dogs. BCS, body condition score; MMS, muscle mass score; MER, metabolic energy requirement. To convert kcal to kJ, multiply by 4.184.

Species: feline/BCS: 5/MMS: 3

Body weight: 3 kg

Food metabolisable energy: 3.90 kcal/g

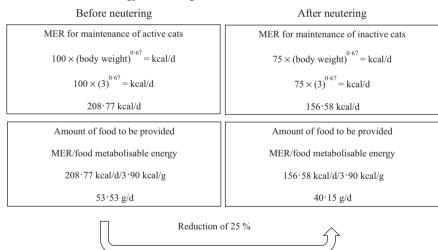


Fig. 3. Effect of neutering on energy requirement for adult cats. BCS, body condition score; MMS, muscle mass score; MER, metabolic energy requirement. To convert kcal to kJ, multiply by 4.184.

satiety, slow-digesting starches are recommended to minimise animal appetite(122) as they provide a prolonged postprandial response to glucose and insulin, which could improve glycaemic

Data available in the literature on the effect of protein on neutered dogs and cats are limited. One study has shown that neutered cats with body weight similar to intact cats may have relatively lower lean body mass⁽¹²³⁾. For example, canine diets with high levels of protein may be a beneficial nutritional strategy to maintain body composition after neutering, with the maintenance of lean mass and not increase of fat mass⁽¹²⁴⁾. However, more studies are needed to verify the impact of different levels of protein intake on pets after neutering.

Based on the information described in the literature to date, Table 1 summarises the metabolic and physiological changes related to neutering and recommended nutritional management for dogs and cats.





Table 1. Physiological changes of neutering and nutritional recommendations for dogs and cats

Item	Recommendation	Justification	References
Energy	Decrease	Neutered animals present decreased energy requirement (due to decreased metabolism and physical activity)	Lund <i>et al.</i> (2005) ⁽¹¹⁹⁾ Bermingham <i>et al.</i> (2010) ⁽¹¹¹⁾ Mitsuhashi <i>et al.</i> (2011) ⁽¹¹²⁾ Bermingham <i>et al.</i> (2014) ⁽¹¹³⁾ Spofford <i>et al.</i> (2014) ⁽¹¹⁸⁾
Protein	Increase	Increased protein may be a beneficial alternative to help maintain lean mass and body composition after neutering	Bjornvad <i>et al.</i> (2011) ⁽¹²³⁾ Kawauchi <i>et al.</i> (2017) ⁽¹²⁴⁾ FEDIAF (2018) ⁽¹¹⁵⁾
Fat	Decrease	Fat is an energy-dense nutrient, hence the content of this nutrient should be decreased after neutering. However, it is extremely important to respect the minimum requirement for dogs and cats	National Research Council (2006) ⁽¹¹⁴⁾ Backus <i>et al.</i> (2007) ⁽¹²⁰⁾ Spofford <i>et al.</i> (2014) ⁽¹¹⁸⁾ Schauf <i>et al.</i> (2016) ⁽¹⁰³⁾
Carbohydrate	Decrease	Dogs and cats do not need dietary carbohydrates. The use of diets with lower amounts of carbohydrates and consequently lower energy density may be useful for the maintenance of ideal body condition	Lund <i>et al.</i> (2005) ⁽¹¹⁹⁾ Backus <i>et al.</i> (2007) ⁽¹²⁰⁾ Carciofi <i>et al.</i> (2008) ⁽¹²²⁾ Schauf <i>et al.</i> (2016) ⁽¹⁰³⁾
Fibre	Increase	Higher concentrations of fibre may be helpful in promoting satiety and decreasing the energy density of diets	National Research Council (2006) ⁽¹¹⁴⁾ Weber <i>et al.</i> (2007) ⁽¹²¹⁾ FEDIAF (2018) ⁽¹¹⁵⁾
Vitamins and minerals	No alteration needed	To date, there is no scientific evidence to recommend modifications in vitamins and mineral content after neutering	National Research Council (2006) ⁽¹¹⁴⁾ FEDIAF (2018) ⁽¹¹⁵⁾

FEDIAF, European Pet Food Industry Federation.

Conclusions

Neutering dogs and cats leads to benefits such as the prevention of undesired reproduction, decreased incidence of neoplasia, and increased life expectancy in dogs and cats. In contrast, neutered animals may be more predisposed to obesity. The higher propensity for weight gain can be prevented by the implementation of adequate nutritional management in the postneutering phase, focusing mainly on the correct calculation of energy requirement and the use of a proper diet. Based on the present review, veterinary professionals now have scientific tools to recommend or not the neutering procedure and the appropriate nutritional management for this purpose.

Acknowledgements

The authors would like to thank Grandfood Industria e Comercio LTDA (Premier Pet), for the partnership and maintenance of the Dog and Cat Nutrition Research Center (CEPEN PET), where the review was prepared.

The study had no funding.

T. H. A. V. and M. A. B. were responsible for planning the review. T. H. A. V., A. R. A., V. P., R. V. A. Z. and R. B. A. R. were responsible for writing and editing. M. A. B. was responsible for reviewing the manuscript.

There are no conflicts of interest to be declared by the authors.

References

1. Kustritz MVR (2002) Early spay-neuter: clinical considerations. Clin Tech Small Anim Pract 17, 124-128.

- 2. Kustritz MVR (2007) Determining the optimal age for gonadectomy of dogs and cats. J Am Vet Med Assoc 231, 1665-1675.
- 3. Howe LM (2006) Surgical methods of contraception and sterilization. Theriogenology 66, 500-509.
- 4. Bailey CS (2016) Non-cancerous conditions associated with spay/neuter status in the canine. Clin Theriogenol 8, 203–206.
- Reichler IM (2009) Gonadectomy in cats and dogs: a review of risks and benefits. Reprod Domest Anim 44, 29-35.
- 6. Houlihan KE (2017) A literature review on the welfare implications of gonadectomy of dogs. J Am Vet Med Assoc **250**, 1155-1166.
- 7. Howe LM (2015) Current perspectives on the optimal age to spay/castrate dogs and cats. J Vet Med Res 6, 171-180.
- Beaver BV (editor) (2001) Canine Behavior: A Guide for Veterinarians. São Paulo: Roca.
- OiE World Organisation for Animal Health (2019) Stray dog population control. https://www.oie.int/index.php?id=169&L= 0&htmfile=chapitre_aw_stray_dog.htm (accessed September
- 10. Berthoud D, Nevison C, Waterhouse J, et al. (2011) The prevalence of neutered pet dogs (Canis familiaris) across countries of the Western world. J Vet Behav 6, 77-78.
- 11. Trevejo R, Yang M & Lund EM (2011) Epidemiology of surgical castration of dogs and cats in the United States. J Am Vet Med Assoc 238, 898-904.
- 12. Frye FL, Dorn CR, Taylor DN, et al. (1967) Characteristics of canine mammary gland tumor cases. J Am Anim Hosp Assoc **3**, 1–12.
- Dorn CR, Taylor DN, Frve FL, et al. (1968) Survey of animal neoplasms in Alameda and Contra Costa Counties, California I. Methodology and description of cases. J Nat Cancer Inst 40, 295-305.
- 14. Schneider RA (1975) A population based animal tumor registry. In Animal Disease Monitoring, pp. 162–172 [DG Ingram, WR Mitchell and SW Martin, editors]. Springfield, IL: Charles C. Thomas.





- 15. Beauvais W, Cardwell JM & Brodbelt DC (2012) The effect of neutering on the risk of mammary tumours in dogs - a systematic review. J Small Anim Pract 53, 314-322.
- Chang SC, Chang TJ, et al. (2005) Prognostic factors associated with survival two years after surgery in dogs with malignant mammary tumors: 79 cases (1998-2002). J Am Vet Med Assoc 227, 1625-1629.
- 17. Itoh T, Uchida K, Ishaikawa K, et al. (2005) Clinicopathological survey of 101 canine mammary gland tumors: differences between small-breed dogs and others. I Vet Med Sci 67, 345-347.
- 18. Brodey RS, Fidler IJ, Howson AE, et al. (1966) The relationship of estrous irregularity, pseudopregnancy, and pregnancy to the development of canine mammary neoplasms. J Am Vet Med Assoc 149, 1047-1049.
- 19. Schneider R, Dorn CR, Taylor DON, et al. (2000) Factors influencing canine mammary cancer development and postsurgical survival. J Natl Cancer Inst 43, 1249-1261.
- Sorenmo KU, Shofer SF, Goldschmidt MH, et al. (2000) Effect of spaying and timing of spaying on survival of dogs with mammary carcinoma. J Vet Intern Med 14, 266-270.
- Henderson BE, Ross R, Bernstein L, et al. (1988) Estrogens as a cause of human cancer: The Richard and Hinda Rosenthal Foundation Award Lecture. Cancer Res 48, 246-253.
- Hulka BS, Edison TL, Lininger RA, et al. (1994) Steroid hormones and risk of breast cancer. Cancer 74, 1111-1124.
- MacMahon B, Cole P, Brown J, et al. (1973) Etiology of human breast cancer: a review. J Natl Cancer Inst 50, 21–41.
- 24. Key TJA & Pike MC (1988) The role of estrogens and prostagens in the epidemiology and prevention of breast cancer. Eur J Cancer Clin Oncol 24, 29-43.
- Waters DJ, Kengerie SS, Maras AH, et al. (2017) 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 224, 25-37.
- Rutteman GR & Misdorp W (1993) Hormonal background of canine and feline mammary tumors. J Reprod Fertil Suppl 47, 483-487.
- 27. Overley B, Shofer FS, Goldschmidt MH, et al. (2005) Association between ovariohysterectomy and feline mammary carcinoma. J Vet Intern Med 19, 560-563.
- Henry CJ (2009) Mammary cancer. In Kirk's Current Veterinary Therapy XIV, 14th ed., pp. 363-368 [JD Bonagura and DC Twedt, editors]. St Louis, MO: Saunders/Elsevier.
- Johnston SD, Root Kustritz MV & Olson PN (editors) (2001) Disorders of the canine testes and epididymes. In Canine and Feline Theriogenology, pp. 312-332. Philadelphia, PA: WB Saunders.
- Towle HA (2012) Testes and scrotum. In Veterinary Surgery: Small Animal, pp. 1906–1907 [KM Tobias and SA Johnston, editors]. St Louis, MO: Saunders/Elsevier.
- 31. Wolke R (1963) Vaginal leiomyoma as a cause of chronic constipation in the cat. J Am Vet Med Assoc 143, 1103–1105.
- 32. Stein B (1981) Tumors of the genital tract. J Am Anim Hosp Assoc 17, 1022-1025.
- Thacher C & Bradley RL (1983) Vulvar and vaginal tumors in the dog: a retrospective study. J Am Vet Med Assoc 183,
- 34. Kydd DM & Burnie AG (1986) Vaginal neoplasia in the bitch a review of 40 clinical cases. J Small Anim Pract 27, 255–263.
- 35. Brodey RS & Roszel JF (1967) Neoplasms of the canine uterus, vagina, and vulva: a clinicopathologic survey of 90 cases. JAm Vet Med Assoc 151, 1294–1307.
- Saba CF & Lawrence JA (2013) Tumors of the female reproductive system. In Withrow MacEwen's Small Animal

- Clinical Oncology eBook, 5th ed., pp. 532–536 [SJ Withrow, DM Vail and RL Page, editors]. St Louis, MO: Elsevier.
- 37. Herron MA (1983) Tumors of the canine genital system. J Am Anim Hosp Assoc 19, 981-994.
- Teske E, Naan EC, Dijk VEM, et al. (2002) Canine prostate carcinoma: epidemiologycal evidence of an increased risk in castrated dogs. Mol Cell Endocrinol 197, 251-255.
- 39. Al Omari R, Shidaifat F & Dardaka M (2005) Castration induced changes in dog prostate gland associated with diminished activin and activin receptor expression. Life Sci 77, 2752-2759.
- Heuter KJ (2008) Diseases of the prostate. In Handbook of Small Animal Practice, 5th ed., pp. 559-568 [RV Morgan, editor]. St Louis, MO: Saunders/Elsevier.
- 41. Bennett PF, Taylor R, Williamson P, et al. (2018) Demographic risk factors for lymphoma in Australian dogs: 6201 cases. J Vet Intern Med 32, 2054-2060.
- 42. Verstegen-Onclin K & Verstegen J (2006) Non-reproductive effects of spaying and neutering: effects on the urogenital system. In Proceedings of the Third International Symposium on Non-Surgical Contraceptive Methods for Pet Population Control, Alexandria, Virginia, November 2016. https://www. acc-d.org/resource-library/symposia/3rd-symposium (accessed December 2019).
- 43. Arnold S (1997) Urinary incontinence in castrated bitches. 2. Diagnosis and treatment. Schweiz Arch Tierheilkd 139, 319-324.
- 44. Spain CV, Scarlett J, Cully S, et al. (2002) When to neuter dogs and cats: a survey of New York State veterinarians' practices and beliefs. J Am Anim Hosp Assoc 38, 482-488.
- Lekcharoensuk C, Osborne CA, Lulich JP, et al. (2001) Epidemiologic study of risk factors for lower urinary tract diseases in cats. J Am Vet Med Assoc 218, 1429-1435.
- Stubbs WP, Bloomberg MS, Scruggs SL, et al. (1996) Effects of prepubertal gonadectomy on physical and behavioral development in cats. J Am Vet Med Assoc 209, 1864–1871.
- 47. Root MV, Johnston SD, Olson PN, et al. (1997) The effect of prepuberal and postpuberal gonadectomy on radial physeal closure in male and female domestic cats. Vet Radiol Ultrasound 38, 42-47.
- Rogers KS (1997) Transmissible venereal tumor. Compend Contin Educ Pract Vet 19, 1036-1045.
- 49. Das U & Das AK (2000) Review of canine transmissible venereal sarcoma. Vet Res Commun 24, 545-556.
- Woods IP (2013) Canine transmissible venereal tumor. In Withrow MacEwen's Small Animal Clinical Oncology eBook, 5th ed., pp. 692-696 [SJ Withrow, DM Vail and RL Page, editors]. St Louis, MO: Elsevier.
- Ware WA & Hopper DL (1999) Cardiac tumors in dogs: 1982-1995. J Vet Intern Med 13, 95-103.
- Hoffman JM, Creevy KE & Promislow DE (2013) Reproductive capability is associated with lifespan and cause of death in companion dogs. PLOS ONE 8, e61082.
- Kent MS, Burton JH, Dank G, et al. (2018) Association of cancer-related mortality, age and gonadectomy in golden retriever dogs at a veterinary academic center (1989-2016). PLOS ONE 13, e0192578.
- 54. Hart BL, Hart LA, Thigpen AP, et al. (2016) Neutering of German shepherd dogs: associated joint disorders, cancers and urinary incontinence. Vet Med Sci 16, 191-199.
- 55. Zink MC, Farhoody P, Elser SE, et al. (2013) Evaluation of the risk and age of onset of cancer and behavioral disorders in gonadectomized Vizslas. J Am Vet Med Assoc 244,
- 56. Sundburg CR, Belanger JM, Bannasch DL, et al. (2016) Gonadectomy effects on the risk of immune disorders in the dog: a retrospective study. BMC Vet Res 12, 278-288.





- Tanriverdi F, Silveira L, Maccoll G, et al. (2003) The hypothalamic-pituitary-gonadal axis: immune function and autoimmunity. J Endocrinol 176, 293-304.
- Grossman CJ (1985) Interactions between the gonadal steroids and the immune system. Science 227, 257-261.
- Ahmed SA, Penhale W & Talal N (1985) Sex hormones, immune responses, and autoimmune diseases. Mechanisms of sex hormone action. Am J Pathol 121, 531-551.
- Moore GE, Guptill LF, Ward MP, et al. (2005) Adverse events diagnosed within 3 days of vaccine administration in pet dogs. J Am Vet Med Assoc 227, 1102-1108.
- 61. Moore GE, DeSantis-Kerr AC, Guptill LF, et al. (2007) Adverse events after vaccine administration in cats: 2,560 cases (2002-2005). J Am Vet Med Assoc 231, 94-100.
- 62. Kim MS, Chae HJ, Shin TY, et al. (2001) Estrogen regulates cytokine release in human mast cells. Immunopharmacol Immunotoxicol 23, 495-504.
- 63. Page ST, Plymate SR, Bremner WJ, et al. (2006) Effect of medical castration on CD4+CD25+ T cells, CD8+ T cell IFN-y expression, and NK cells: a physiological role for testosterone and/or its metabolites. Am J Physiol Endocrinol Metab 290, 856-863
- Johnson AB & Sohrabji F (2005) Estrogen's effects on central and circulating immune cells vary with reproductive age. Neurobiol Aging 26, 1365-1374.
- Salmeri K, Bloomberg M, Scruggs SL, et al. (1991) Gonadectomy in immature dogs: effects on skeletal, physical, and behavioral development. J Am Vet Med Assoc 198,
- Kustritz MVR (2012) Effects of surgical sterilization on canine and feline health and on society. Reprod Domest Anim 47, 214-222.
- Torres De La Riva G, Hart BL, Farver TB, et al. (2013) Neutering dogs: effects on joint disorders and cancers in golden retrievers. PLOS ONE 8, e55937.
- Hart BL, Hart LA, Thigpen AP, et al. (2014) Long-term health effects of neutering dogs: comparison of Labrador retrievers with golden retrievers. PLOS ONE 9, e102241.
- Ekenstedt KJ (2017) DNM1 mutation status, sex, and sterilization status of a cohort of Labrador retrievers with and without cranial cruciate ligament rupture. Canine Genet Epidemiol 4, 2.
- McNicholas WT, Wilkens BE, Blevins WE, et al. (2002) Spontaneous femoral capital physeal fractures in adult cats: 26 cases (1996–2001). J Am Vet Med Assoc 221, 1731–1736.
- 71. Perry KL, Fordham A & Arthurs GI (2014) Effect of neutering and breed on femoral and tibial physeal closure times in male and female domestic cats. J Feline Med Surg 16, 149-156.
- Hart BL & Eckstein RA (1997) The role of gonadal hormones in the occurrence of objectionable behaviours in dogs and cats. Appl Anim Behav Sci 52, 331-344.
- Patronek GJ, Glickman LT, Beck AM, et al. (1996) Risk factors for relinquishment of dogs to an animal shelter. J Am Vet Med Assoc 209, 572-581.
- 74. Spain CV, Scarlett JM, Houpt KA, et al. (2004) Long-term risks and benefits of early-age gonadectomy in cats. J Am Vet Med Assoc 224, 372-379.
- 75. Hopkins SG, Schubert TA, Hart BL, et al. (1976) Castration of adult male dogs: effects on roaming, aggression, urine marking, and mounting. J Am Vet Med Assoc 168, 1108-1110.
- 76. Nielsen JC, Eckstein RA, Hart BL, et al. (1997) Effects of castration on problem behaviors in male dogs with reference to age and duration of behavior. J Am Vet Med Assoc 211,
- 77. Hart BL & Barrett RE (1973) Effects of castration on fighting, roaming, and urine spraying in adult male cats. J Am Vet Med Assoc 163, 290-292.

- 78. Duffy DL, Hsu YY & Serpell JA (2008) Breed differences in canine aggression. Appl Anim Behav Sci 114, 441-460.
- 79. Farhoody P, Mallawaarachchi I, Tarwater PM, et al. (2018) Aggression toward familiar people, strangers, and conspecifics in gonadectomized and intact dogs. Front Vet Sci 26, 5-18.
- 80. Scandurra A, Alterisio A, Di Cosmo A, et al. (2019) Ovariectomy impairs socio-cognitive functions in dogs. Animals (Basel) 9, E58.
- Valcke A (2017) Prepubertal gonadectomy in cats: long-term effects on behaviour. Masters Thesis, Ghent University.
- Janowsky JS (2006) The role of androgens in cognition and brain aging in men. Neuroscience 138, 1015-1020.
- Waters DJ, Shen S, Glickman LT, et al. (2000) Life expectancy, antagonistic pleiotropy, and the testis of dogs and men. Prostate 43, 272-277.
- 84. Gibbs RB & Johnson DA (2008) Sex-specific effects of gonadectomy and hormone treatment on acquisition of a 12-arm radial maze task by Sprague Dawley rats. Endocrinology **149**, 3176-3183.
- 85. Spritzer MD, Gill M, Weinberg A, et al. (2008) Castration differentially affects spatial working and reference memory in male rats. Archiv Sex Behav 37, 19-29.
- 86. Spritzer MD, Daviaub ED, Coneenya MK, et al. (2011) Effects of testosterone on spatial learning and memory in adult male rats. Horm Behav 59, 484-496.
- 87. Wagner BA, Braddick VC, Batson CG, et al. (2017) Effects of testosterone dose on spatial memory among castrated adult male rats. Psychoneuroendocrinology 89, 120-130.
- Mongillo P, Scandurra A, D'Aniello B, et al. (2017) Effect of sex and gonadectomy on dogs' spatial performance. Appl Anim Behav Sci 191, 84-89.
- Spain CV, Scarlett JM & Houpt KA (2004) Long-term risks and benefits of early-age gonadectomy in cats. J Am Vet Med Assoc **224**, 372–379
- 90. McGreevy PD, Wilson B, Starling MJ, et al. (2018) Behavioural risks in male dogs with minimal lifetime exposure to gonadal hormones may complicate population-control benefits of desexing. PLOS ONE 13, e0196284.
- 91. Burrow R, Batchelor D, Cripps P, et al. (2005) Complications observed during and after ovariohysterectomy of bitches at a veterinary teaching hospital. Vet Rec 157, 829-833.
- 92. Pollari FL, Bonnett BN, Bamsey SC, et al. (1996) Postoperative complications of elective surgeries in dogs and cats determined by examining electronic and paper medical records. I Am Vet Med Assoc 208, 1882-1886.
- 93. Epstein ME, Rodan I, Griffenhagen G, et al. (2015) AAHA/AAFP pain management guidelines for dogs and cats. J Feline Med Surg 17, 251-272.
- 94. American College of Veterinary Anesthesia and Analgesia (2016) American College of Veterinary Anesthesiologists' position paper on the treatment of pain in animals. https:// www.acvaa.org/docs/Pain_Treatment (accessed September 2019)
- 95. de Godov MRC (2018) Pancosma comparative gut physiology symposium: all about appetite regulation: effects of diet and gonadal steroids on appetite regulation and food intake of companion animals. J Anim Sci 96, 3526-3536.
- 96. Fettman MJ, Stanton CA, Banks LL, et al. (1997) Effects of neutering on bodyweight, metabolic rate and glucose tolerance of domestic cats. Res Vet Sci 62, 131-136.
- 97. Houpt KA, Coren B, Hintz HF, et al. (1979) Effect of sex and reproductive status on sucrose preference, food intake and body weight of dogs. JAm Vet Med Assoc 174, 1083-1085.
- Jeusette I, Detilleux J, Cuvelier C, et al. (2004) Ad libitum feeding following ovariectomy in female Beagle dogs: effect on maintenance energy requirement and on blood metabolites. J Anim Physiol Anim Nutr 88, 117-121.





- Butera PC (2010) Estradiol and the control of food intake. Physiol Behav 99, 175-180.
- 100. Kanchuk M, Backus RC, Calvert CC, et al. (2003) Weight gain in gonadectomized normal and lipoprotein lipasedeficient male domestic cats results from increased food intake and not decreased energy expenditure. J Nutr 133, 1866-1874
- 101. Mystkowski P & Schwartz MW (2000) Gonadal steroids and energy homeostasis in the leptin era. Nutrition 16, 937-946.
- 102. Allaway D, Gilham M, Colyer A, et al. (2017) The impact of time of neutering on weight gain and energy intake in female kittens. I Nutr Sci 6, e19.
- Schauf S, Salas-Mani A, Torre C, et al. (2016) Effect of sterilization and of dietary fat and carbohydrate content on food intake, activity level, and blood satiety-related hormones in female dogs. J Anim Sci 94, 4239-4250.
- Michel KE (2012) Nutritional management of body weight. In Applied Veterinary Clinical Nutrition, pp. 109-124 [AJ Fascetti and SJ Delaney, editors]. Chichester: Wiley-Blackwell.
- 105. Panciera DL, Thomas CB, Eicker SW, et al. (1990) Epizootiologic patterns of diabetes mellitus in cats: 333 cases (1980–1986). J Am Vet Med Assoc 197, 1504–1508.
- 106. McCann TM, Simpson KE, Shaw DJ, et al. (2007) Feline diabetes mellitus in the UK: the prevalence within an insured cat population and a questionnaire-based putative risk factor analysis. I Feline Med Surg 9, 289-299.
- Prahl A, Guptill L, Glickman NW, et al. (2007) Time trends and risk factors for diabetes mellitus in cats presented to veterinary teaching hospitals. J Feline Med Surg 9, 351-358.
- Hoenig M & Ferguson DC (2002) Effects of neutering on hormonal concentrations and energy requirements in male and female cats. Am J Vet Res 63, 634-639.
- Kanchuk ML, Backus RC, Calvert CC, et al. (2002) Neutering induces changes in food intake, body weight, plasma insulin and leptin concentrations in normal and lipoprotein lipasedeficient male cats. J Nutr 132, 1730-1732.
- 110. Le Roux PH (1983) Thyroid status, oestradiol level, work performance and body mass of ovariectomised bitches and bitches bearing ovarian autotransplants in the stomach wall. IS Afr Vet Assoc **54**, 115–117.
- 111. Bermingham EN, Thomas DG, Morris PJ, et al. (2010) Energy requirements of adult cats. Br J Nutr 103, 1083-1093.

- 112. Mitsuhashi Y, Chamberlin AJ, Bigley KE, et al. (2011) Maintenance energy requirement determination of cats after spaying. Br J Nutr 106, 135-138.
- Bermingham EN, Thomas DG, Cave NC, et al. (2014) Energy requirements of adult dogs: a meta-analysis. PLOS ONE 9, e109681.
- 114. National Research Council (2006) Nutrient Requirements of Dogs and Cats. Washington, DC: National Research Council of the National Academies.
- 115. FEDIAF (European Pet Food Industry Federation) (2018) Nutritional Guidelines for Complete and Complementary Pet Food for Cats and Dogs. Brussels: European Pet Food Industry Federation.
- Colliard L, Paragon BM, Lemuet B, et al. (2009) Prevalence and risk factors of obesity in an urban population of healthy cats. J Feline Med Surg 11, 135-140.
- 117. WSAVA Nutritional Assessment Guidelines Task Force Members (2011) WSAVA nutritional assessment guidelines. J Small Anim Pract 52, 385-396.
- 118. Spofford N, Mougeot V, Elliott DA, et al. (2014) A moderate fat, low-energy dry expanded diet reduces gain in body condition score when fed as part of a post neutering weight-control regimen in growing pet cats. J Nutr Sci 3, e40.
- Lund EM, Armstrong PJ, Kirk CA, et al. (2005) Prevalence and risk factors for obesity in adult cats from private U.S. veterinary practices. Int J Appl Res Vet Med 3, 88-96.
- Backus RC, Cave NJ & Keisler DH (2007) Gonadectomy and high dietary fat but not high dietary carbohydrate induce gains in body weight and fat of domestic cats. Br J Nutr 98, 641-650.
- Weber M, Bissot T, Servet E, et al. (2007) A high-protein, high-fiber diet designed for weight loss improves satiety in dogs. J Vet Intern Med 21, 1203-1208.
- 122. Carciofi AC, Takakura FS, De-Oliveira LD, et al. (2008) Effects of six carbohydrate sources on dog diet digestibility and post-prandial glucose and insulin response. J Anim Physiol Anim Nutr 92, 326-336.
- 123. Bjornvad CR, Nielsen DH, Armstrong PJ, et al. (2011) Evaluation of a nine-point body condition scoring system in physically inactive pet cats. Am J Vet Res 72, 433-437.
- 124. Kawauchi IM, Jeremias JT, Takeara P, et al. (2017) Effect of dietary protein intake on the body composition and metabolic parameters of neutered dogs. J Nutr Sci 6, e40.

