Review

Evaluating the benefits and risks of neutering dogs and cats

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Abstract

Neutering consists of removing the source of the hormones that control reproduction and determine secondary sexual characteristics. In dogs and cats, this is most commonly accomplished by castration or ovariectomy. While the primary purpose of neutering is to prevent reproduction, the procedure may have other physical and behavioural effects.

Epidemiologic research has identified many beneficial and harmful outcomes associated with neutering. A definitively causal relationship between these outcomes and neuter status cannot be accepted without consistent evidence from multiple studies of adequate size and quality. However, consideration of the possible health consequences of these associations is warranted when offering owners recommendations concerning neutering.

An evidence-based decision about neutering a particular pet requires integrating relevant research data with the veterinarian's clinical expertise and the needs and circumstances of the patient and owner. It is impossible to precisely predict the outcome of neutering for any individual. However, existing research does allow some generalization about the magnitude and clinical importance of specific risks and benefits. Overall, it appears justified to recommend spaying all females not intended for breeding, because the procedure is more likely to prevent rather than cause disease. In male dogs, the benefits of castration are not so clearly greater than the risks. The evidence is also mixed regarding the risks and benefits of neutering dogs before 5–6 months of age, and so no strong recommendation for or against the practice can be made. However, it is clear that spaying female dogs before their first heat is preferable to spaying them later.

Keywords: Cat, Dog, Castration, Spaying, Neuter, Risks, Benefits

Review Methodology: The literature was identified by keyword search of the following databases: Pubmed and Medline. Additional articles were identified by keyword search of the Veterinary Information Network and Google and by examining the references of articles identified for further relevant material. Keywords for electronic searches included the following as well as combinations and variants thereof: cat, dog, spay, castration, neuter, risk factors, risks, benefits.

Introduction

Neutering consists of removing the source of the hormones that control reproduction and that determine the typical physical and behavioural characteristics that distinguish males and females. In dogs and cats, this is most commonly accomplished by surgically removing the testicles in males (castration) and the ovaries in females (spaying), though there are a variety of surgical techniques as well as non-surgical methods of contraception to prevent reproduction without removing the source of gonadal hormones [1, 2]. There is significant variation among countries, regions and communities in specific neutering practices, in the proportion of owned cats and dogs that are neutered, and in the attitudes among pet owners and veterinarians towards neutering [3-7].

While the primary purpose of surgical neutering is to prevent reproduction, like most medical interventions, the procedure has other effects, both beneficial and undesirable. Making a rational, evidence-based decision about neutering a pet requires integrating the research evidence concerning the benefits and the risks of the procedure with the veterinarian's clinical expertise and the needs and circumstances of the individual patient and owner. Veterinarians, breeders and pet owners often have strong opinions about neutering, and unfortunately these are all too often based on tradition, habit, rumour or misconception. There is a large and complex scientific literature addressing the risks and benefits of neutering, and a number of reviews of this information have appeared in scientific publications or have been posted on the Internet by interested laypersons [8–15].

Though there are many studies that consider the impact of neutering on disease risk, they have limitations which affect the applicability of the data and conclusions they generate to individual patients. Large-scale prospective studies are rare, and even in these there are practical difficulties in controlling for confounding variables. Most of the studies which examine the possible influence of neutering on health and disease are retrospective observational studies with or without controls, and these often have significant limitations in determining the aetiological significance of the risk factors identified [16]. Many factors must be considered in evaluating the applicability of associations detected in observational studies to other populations or individual patients, including the size and composition of the study population, the study design, the appropriateness of statistical methods and the potential influence of confounding variables [17].

Another issue to consider in interpreting studies about the risks and benefits of neutering is how these risks are described. Differences between groups are often described in terms of relative risk. However, it is frequently difficult to determine from published studies the underlying absolute risk, which is critical to rational clinical risk analysis. Relative risk figures alone tend to exaggerate the perception of benefit and harm associated with risk factors [18, 19]. I have attempted, whenever possible, to provide figures for the incidence of disease conditions which may be affected by neutering, though unfortunately the true incidence of most conditions seen in veterinary medicine is not known.

In addition to the incidence of a clinical disorder associated with the neuter status, it is important to consider the clinical impact of the disorder and how amenable it is to treatment, since these factors may influence how relevant the risk of a disorder is to any decision about neutering a particular patient. This review is an attempt to consider the totality of the scientific information currently available and to draw some pragmatic conclusions about the overall benefits and risks of neutering dogs and cats.

Benefits of Neutering

Population Benefits

The primary benefit of neutering is the prevention of unintended reproduction. Though the number of unwanted cats and dogs euthanized at animal shelters in the USA has decreased from an estimated 23.4 million in 1970 to about 4.5 million by the year 2000 [20], this still represents a significant animal welfare concern. Reducing the total number of unwanted puppies and kittens remains important in reducing the relinquishment and euthanasia of these animals, and failure to neuter is an important component of the pet population problem [21, 22]. Furthermore, intact cats and dogs are at an increased risk of being given up by their owners, possibly because they exhibit unacceptable behaviours associated with being intact or because they result from unintended reproduction or are surplus offspring of other pets in the household. [23-26]. So neutering can reduce the number of unwanted puppies and kittens and the risk of owned animals being relinquished.

The feral or stray cat population, though notoriously difficult to assess, contains an estimated 30–40 million animals in the USA, most the product of unplanned breeding [20]. There is a great deal of controversy over the welfare of feral cats and the impact they may have on wildlife and public health [27–30]. It is generally agreed, however, that feral cats suffer more disease and parasitism and have shorter lives than owned cats and that reducing the number and reproduction of cats not owned is a worthwhile goal [31]. Neutering of owned and feral cats, can promote this goal, though it is likely that neutering programmes alone cannot fully control cat populations or reliably eliminate feral colonies [29, 32, 33].

While populations of stray dogs have largely been eliminated in the USA and much of Europe, such populations still exist in many countries and represent a significant human health hazard [20, 34, 35]. There are many factors involved in controlling stray dog populations and the health risk they present [34, 36]. Research suggests that neutering alone is insufficient to control stray dog populations, but it is widely considered a vital component in such efforts [34, 35, 37–39].

Risks of Reproduction

Reproduction itself has potential risks which can be eliminated by neutering. Dogs of both sexes are susceptible to infection with *Brucella canis*, a bacterium which can cause disease in dogs and humans. This bacterium can be transmitted during breeding or acquired from contact with aborted foetuses and other material from infected females. The incidence of this disease varies by country and region, from 1–18% in USA to 25% and above in some countries. Clinical symptoms other than infertility are uncommon, though some dogs experience serious infections of the bone, eyes or nervous system [31].

The most common complication of pregnancy for females is dystocia. Rates of dystocia in dogs vary greatly by breed, from as low as 5% of whelpings to over 85%

in breeds with large heads [40]. One study in Sweden, using information from an insurance database of approximately 200 000 female dogs, most of which were intact, found that 2% female dogs in the sample experienced a dystocia, and the overall incidence was 5.7 cases/ 1000 dog years at risk [41]. The study population consisted of dogs covered by health insurance, and so it may or may not be applicable to dogs in other countries or those whose owners do not utilize pet health insurance.

In cats, the risk of dystocia also varies by breed, with one study reporting an overall rate of 5.8% of deliveries, ranging from 0.4% in a colony of mixed breed cats to 18.2% for Devon rex cats [42].

Though dystocia can be treated medically, the majority of dogs and cats require surgical treatment [40–43]. Most females recover fully from caesarean sections, though the risks of such surgery are likely greater than those of a planned spay surgery because of the emergency nature of the procedure and the often compromised health of the female secondary to the dystocia. In breeds with a high risk for dystocia, elective caesarean section can often be performed to prevent dystocia, which is safer than emergency surgery once dystocia has developed.

Much less common risks of pregnancy, such as pregnancy toxaemia, diabetes mellitus, uterine torsion, uterine rupture and pregnancy-associated pyelonephritis can all be prevented by neutering in both dogs and cats [43].

Mammary Neoplasia

Mammary tumours are very common in intact female dogs. The chances of developing a mammary tumour increase with age and vary with breed [43, 44]. Incidence is reported in a number of different ways, which makes comparison between studies difficult. A study in Norway, where almost all female dogs are intact, found a crude incidence of malignant mammary tumours of 53.3%, with significant variation in risk by breed and age [45]. A study in the UK, looking at a population of both intact and spayed dogs in a health insurance database, found mammary tumours to be the second most common type of tumour, with an age standardized incidence of 205 tumour per 100 000 dogs per year; however, no breakdown of this figure according to the neuter status was reported [46]. A Swedish study found an incidence in intact females of 1% at 6 years of age, 6% at 8 years and 13% at 10 years (when the study was terminated) [47]. The incidence of mammary tumours in female cats is roughly half that seen in dogs, and there is no apparent protective effect of having a litter for dogs or cats [44, 48]. Mammary neoplasia is extremely rare in male dogs [44].

About half of the canine mammary tumours are malignant, whereas 85–90% of the feline mammary tumours are malignant [44, 49]. Mammary cancer is usually treated surgically, often with adjunctive post-surgical chemotherapy, and it is often fatal despite treatment, with 59% dogs with malignant tumours in one study eventually dying of causes related to their cancer [50].

Spaying dramatically reduces the risk of mammary tumours in both dogs and cats. In dogs the risk has been reported as 0.5% for females spayed before the first oestrus, 8% for those spayed before the second oestrus and 26% for those spayed after the second oestrus [51]. One study in cats found those spayed prior to 6 months of age had a 91% reduction in mammary cancer risk, and the risk was reduced by 86% in those spayed before 1 year [48]. Spaying dogs later than the third oestrus does not reduce the risk of developing mammary cancer, but spaying at the time of surgical removal of the mammary tumour or within 2 years before the diagnosis of mammary cancer is associated with longer survival [50].

Pyometra

Pyometra is a bacterial infection of the uterus that occurs as a consequence of changes in the uterine environment brought about by repeated oestrus cycles [43]. Pyometra can be treated medically, with resolution of infection reported in 46–95% cases, with minimal short-term complications, and with relatively high rates of recurrence (20–28%) and subsequent fertility problems [52–58]. It is more commonly treated, and recurrence prevented, by spaying the affected dog [43, 55].

A study in Sweden, where elective spaying is rarely practiced, found that overall 25% of the females in the study developed pyometra by 10 years of age, and it was expected the risk would continue to increase in even older females. The risk varied considerably by breed, with some breeds having a 10% rate of pyometra and others up to 50%. Risk increased with age for all breeds [59]. Pyometra has been reported in cats, but no published figures regarding the incidence are available.

Mortality from pyometra treated surgically is variable, from 4.2 to 17% in dogs and 8% in cats [43]. Mortality rates associated with medical treatment of pyometra were not identified. However, such treatment would not be appropriate for critically ill patients, and so the mortality rate would be expected to be lower for medically treated cases since significantly compromised individuals would likely be treated surgically.

Spaying essentially eliminates the risk of pyometra in dogs and cats. Uterine stump pyometras do occur if some ovarian tissue or other source of progesterone is present, but this is rare [43]. Ovariectomy is as effective as ovariohysterectomy in preventing pyometra [60].

Neoplasia of Reproductive Organs

Tumours of the ovaries are uncommon in dogs and cats with reported incidences of 6.25% in dogs and between

0.7 and 3.6% in cats. There are several different types of ovarian tumours with variable degrees of malignancy. Little reliable information exists regarding the mortality associated with these tumours [61].

Uterine tumours are very rare in dogs and cats, accounting for less than 2% of feline tumours and less than 0.5% of all canine tumours. Tumours of the uterus can generally be successfully removed by spaying the animal, though recurrence and spread to other organs have been reported [61].

Tumours of the vulva or vagina in female dogs are not common, though they represent 2-3% of all canine tumours. They occur primarily in intact females and often have receptors for ovarian hormones, and they are less likely to recur in dogs spayed at the time of tumour removal [61–64]. This suggests that the risk of such tumours is decreased in spayed females. Most vulvar and vaginal tumours are benign and can be cured by surgical removal, though the minority that are malignant have a poor prognosis and often recur or metastasize [61].

Various rates of occurrence have been reported for testicular tumours, but random samples of testicles from dogs autopsied for reasons not related to testicular disease have shown that 16–27% dogs had tumours, and many of these had more than one [65]. The testicles are the second most common site for cancer in intact male dogs [66]. Cryptorchid testicles are more likely to develop tumours, especially in dogs under 10 years of age [67, 68].

There are several types of testicular tumours. Most are slow to metastasize, with less than 15% affected dogs showing spread to other organs. Some testicular tumours produce hormones, including oestrogen which can cause feminization and bone marrow hypoplasia. Castration is the treatment of choice for testicular neoplasia, and it is usually curative [43, 61].

Prostate Disease

The most common disease of the canine prostate is benign prostatic hyperplasia (BPH) [43, 69]. The incidence of this disorder increases with age, from 15–40% for dogs under 7 years of age to 60–100% for dogs over 7 years of age [69–71]. While most dogs have a few symptoms from BPH, some experience difficulty urinating or defecating or have bloody preputial secretions. BPH is a predisposing and complicating factor for prostatitis [43]. Prostatitis has been reported to occur in up to 28.5% intact male dogs [69, 72]. It is a serious and uncomfortable disease, though rarely life-threatening. Both BPH and prostatitis are rare in neutered dogs and both are effectively prevented and treated by castration [43, 69].

Behavioural Benefits

Behavioural problems are an important reason for relinquishment of pet dogs and cats by owners [20, 27, 73]. The most common problem behaviours include aggression towards people or other animals, inappropriate elimination and fearful behaviours [74]. To the extent that neutering increases or reduces the risks for these behaviours it can have an important impact on the relationship between pet and owner and ultimately on the pet's survival.

The biological and environmental influences on animal behaviour are complex and difficult to unravel, so epidemiological correlations are unreliable in predicting the outcome of interventions in individual cases. Most of the literature concerning neutering and behaviour is consistent of owner surveys or analyses of biting or other problem behaviours reported to animal control agencies or shelters. These studies have significant methodological limitations as they are generally observational and retrospective, and often involve sample populations that may not be truly representative of dogs and cats generally. However, there are some consistent patterns that emerge from studies on normal and problem behaviours in dogs and cats which illustrate the potential behavioural benefits and risks associated with neutering.

Most studies have found intact male dogs to be disproportionately involved in aggressive behaviour [75–77]. Others have reported marked reductions in aggression and other problem behaviours in male dogs as an effect of castration. In one study, roaming behaviour decreased 90%, aggression between males decreased 62%, urine marking decreased 50% and mounting decreased 80% following castration [78], and several other studies have found similar results [79–81]. Some studies have also reported intact dogs to be more likely to bite humans than neutered animals [77].

Castration also dramatically reduces fighting, urine spraying and roaming in male cats [81–83]. One of the few experimental, prospective studies in this area compared various physical and behavioural characteristics of kittens neutered at 7 weeks of age, others neutered at 7 months of age and a control group left intact. This study found intact cats to be more aggressive towards other cats and less affectionate towards humans than neutered cats [84].

Miscellaneous Benefits

Almost every veterinary epidemiologic study of any disease examines differences in incidence between males and females and intact and neutered animals. If a significant correlation is found, this may or may not have meaningful clinical implications. There are likely many more such associations reported than are listed here, but these are some that have clear significance when considering whether or not to neuter and about which pet owners often have questions and concerns.

Perineal hernias are uncommon in dogs, but no precise incidence has been reported. In one study, 93% of the cases were intact males, and an association with prostatic disease and prostatic hormones is suspected, and so neutering is likely to be protective for this disorder [85, 86]. Perineal hernias can be repaired surgically, with a recurrence reported in from 20 to 40% patients. Castration at the time of initial repair is often recommended, because it may reduce the rate of recurrence, especially in dogs with concurrent prostatic disease [87, 88].

Perianal fistulas is an immune-mediated disease seen most commonly in German Shepherds and Irish Setters and rarely in other breeds. It occurs predominantly in intact male dogs, which suggests a hormonal influence though a specific causal connection has not been identified. In one study, males outnumbered females 2:1 and intact dogs were 86% of the affected patients [89]. Perianal fistulas are chronic and often cause significant discomfort. A variety of medical and surgical treatments are used, with reports of long-term resolution of the condition in from 30 to 78% of cases [90–92].

There is some suggestion in research on laboratory animals as well as retrospective epidemiologic studies of dogs and cats that neutered animals may live longer than intact animals, though the effect is not large or consistent across studies [93-99]. There has been one retrospective survey study of Rottweiler dogs which found an association between the length of time females remained intact and their odds of achieving exceptional longevity (defined as a lifespan \geq 13 years) [100]. However, a previous survey study from the same population reported that intact females lived on an average for 7.5 years, compared with 9.8 years for spayed females [101]. The implications of these studies for other breeds or for any general relationship between lifespan and neuter status are not clear. Also, the possible effects of differences in the care neutered and intact animals receive, genetic factors and many other variables have not been evaluated, which complicates any interpretation of differences in longevity. Therefore, no firm conclusions can be drawn about the effect of neutering on longevity.

Risks of Neutering

Surgical Risks

Like all surgeries, neutering involves some risk of perioperative complications. Total complication rates for routine castration or spaying have been reported from 2.6% to 20% of the cases [102–105]. The majority of these are minor and require no treatment [102, 105]. Complication rates vary considerably from practice to practice and are generally reported to be higher in studies of surgeries performed by students in training [102, 105]. Reported death rates are less than 0.1% [102].

Neoplasia

Prostate cancer in dogs has previously been reported to have an incidence of less than 1% [43], but several recent studies have suggested it may be more common, though not always clinically recognized, and these papers have reported rates of 3.6-13% [69, 72]. Most such cancers are malignant, with metastases reported in 40-80% of the cases at the time of diagnosis [43, 106]. There is some uncertainty about the role of castration in prostate cancer development. All the studies have been retrospective epidemiologic surveys of a relatively small number of dogs with prostatic carcinoma (n=7-76). Some have found fewer prostate cancers in castrated dogs than in intact dogs [106-108]. However, others have found either no effect of castration on the rate of prostate cancers [109] or an increased risk for castrated dogs [72, 110]. Canine prostatic adenocarcinomas arise predominantly from androgen-independent ductal epithelial cells, and so it appears that, unlike in humans, androgens are not responsible for the initiation or progression of prostatic cancers. However, it is unclear whether, overall, castration is beneficial, neutral or a risk factor for the development of prostate cancer [67, 110]. Prostate cancer is an aggressive cancer with a poor long-term prognosis [67].

Osteosarcoma is a bone tumour usually seen in large breed dogs [111, 112]. The overall incidence has been reported as 0.2%, but for at-risk breeds rates of 4.4-6.2% are often reported [8, 113]. A rate of 12.5% was reported in one study of Rottweilers, though the authors suggested this might have been an overestimate [101]. Neutered dogs have been reported to be at higher risk for osteosarcoma than intact dogs [101, 111]. In the study of Rottweilers, no difference was found in the overall risk for intact versus neutered animals of either sex, but neutering before 1 year of age was found to increase the risk, and it was found that the longer an individual had been intact the lower their osteosarcoma risk [101]. However, the neutered animals in this study (especially the spayed females) lived longer than the intact animals, which may have contributed to an increased incidence of cancer in the neutered group.

It is possible that neutering, especially before sexual maturity, raises the risk of osteosarcoma, at least in predisposed breeds. Osteosarcoma is an aggressive cancer with a poor long-term prognosis, and it is generally treated with surgery and chemotherapy [112].

Hemangiosarcoma is a malignant neoplasm of vascular endothelial cells [114]. The true incidence has not been reported, but it makes up 5% of all non-skin cancers in dogs [114]. It is less common in the cat, found in 0.5% cats autopsied and 2% of cancers in this species [114]. It most commonly originates in the spleen, and certain breeds (such as German Shepherds, Labrador Retrievers and Golden Retrievers) are at greater risk than others [114–116]. Primary cardiac hemangiosarcoma may also occur, with a reported incidence of 0.19% [117]. In dogs, spayed females have been reported to have 2 times the risk of splenic hemangiosarcoma and 5 times the risk of cardiac hemangiosarcoma compared with intact females [115, 117]. Castrated males have been found to have no increased risk of splenic hemangiosarcoma [115] and only a slightly higher risk than that of intact males for cardiac hemangiosarcoma [117]. Hemangiosarcoma is an aggressive cancer with a poor long-term prognosis, and it is usually treated by splenectomy (if this is the primary site) and chemotherapy [114].

Transitional cell carcinoma is a cancer of the lower urinary tract, usually found in the bladder and uncommonly in the urethra of dogs [118]. It represents 1-2% of canine cancers and is rare in the cat [118, 119]. It is more common in females than males, prevalence varies by breed, and neutered animals have been reported to be at 2-4 times greater risk than intact animals [119, 120]. Transitional cell carcinoma is an aggressive cancer with a fair long-term prognosis, and it is usually treated with chemotherapy and sometimes surgery or radiation therapy [118].

Orthopaedic Disease Risk

Rupture of the cranial cruciate ligament in the stifle is a common problem of large and giant breed dogs, with an overall incidence of 1.8-4.5%, though the incidence in predisposed breeds has been reported to be as high as 8.9% [121–124]. In addition to breed and obesity, neutering increases the risk of cranial cruciate ligament rupture [121–124]. One retrospective case control study found that in dogs affected by cranial cruciate ligament disease, those neutered before 6 months of age were more likely to have an excessive tibial plateau angle than those neutered later [125]. Cruciate ligament rupture is treated with a variety of surgical approaches, and it has an excellent long-term prognosis [126, 127].

Hip dysplasia is a developmental abnormality of the hip joint that can result in arthritis and clinical discomfort. It is rare in small breeds, with less than 1% of the dogs affected, but it can be seen in as many as 40–75% of large breed dogs [124, 128–130]. Hip dysplasia is estimated to lead to clinically significant arthritis is less than 5% of the affected dogs, but there are many factors involved including breed, weight and the degree of anatomic abnormality of the hip joint, which makes predicting the outcome for any individual difficult [130]. The incidence of hip dysplasia is most strongly associated with breed and family history [124, 131, 132].

Some studies have identified neutering as increasing the risk of hip dysplasia [124, 133]. The age at neutering may also be a factor influencing the development of hip dysplasia [9]. It is unclear if the increased risk is directly the result of the effects of neutering or of an increased incidence of obesity in neutered dogs. Hip dysplasia can be treated if detected early with surgical therapies that reduce the chances of clinically significant arthritis later in life [134, 135]. In older dogs that have already developed arthritis and clinical symptoms, these can be managed surgically or medically, with medications, weight reduction and other therapies [136–138]. Because of the genetic basis of the disorder, the ideal approach to eliminating it is to neuter those dogs that carry the predisposing genes, if they can be identified prior to breeding [139, 140].

A number of studies have found a large majority of spontaneous femoral capital physeal fractures in cats occur in obese neutered males [141–144]. It is clear that neutering delays closure of the growth plates in male cats [145], and so it may be an independent risk factor for such fractures, though neutering also increases the incidence of obesity, and the relative contribution of obesity and neutering to the risk of these fractures has not been elucidated.

Behavioural Risks

Though neutering has generally been associated with a decreased incidence of some kinds of aggression, there is also limited evidence that it may be associated with an increase in some aggressive behaviour. A number of studies of dogs referred for treatment of behaviour problems have identified a higher proportion of spayed than intact females among animals exhibiting aggression [75, 77]. Another study, in which breed club members were surveyed and an open-access web-based owner survey was conducted, found more aggression towards humans and other dogs in spayed than intact females [146]. However, without matched control groups or information about the ratio of intact and neutered male and female dogs in the general populations from which the study subjects were drawn, it is not possible to definitively assess if neutering is associated with more aggression in females, or whether any such association might be causal.

Another study found that if female dogs under 6 months of age showed human-directed aggression prior to being spayed, this aggression became worse after ovariohysterectomy, though aggressive behaviours were not observed in those females who were spayed and had not shown aggressive tendencies prior to the procedure [147]. However, there were differences between the control group and the spayed dogs in addition to having surgery, which make it difficult to generalize from these results.

One survey of Springer Spaniel owners identified more owner-directed aggression reported in dogs that were neutered than in intact dogs [148]. How reliable such an owner survey might be or how applicable to other breeds, is unclear.

One study found female German Shepherds who were neutered were more reactive to the presence of

unfamiliar humans and dogs than were intact dogs [149]. Another study found neutered dogs to be more active than intact dogs and castrated males to be more excitable than intact males, but found no other measurable behavioural differences between the groups [150]. The clinical significance or applicability of these findings to behaviour problems is unclear.

One study has examined the relationship between neutering and the development of age-related behavioural changes thought to be similar to Alzheimer's disease or other forms of senile dementia in humans [151]. Such changes are relatively common, being reported in 28% of dogs at 10-12 years old and 68% of dogs at 15-16 years old [152]. When multiple comparisons were made between intact males, castrated males and spayed females (no intact females were included in the study), the only association found was that when castrated male and spayed female dogs were combined and compared with sexually intact males, the percentage of intact males that progressed from mild to severe cognitive impairment was significantly lower than the percentage of neutered dogs that progressed [152]. It is unlikely that this limited finding has great significance in terms of the overall risk for the development of cognitive dysfunction in neutered or intact dogs.

Miscellaneous Risks

Urinary incontinence is common in middle-aged to older spayed female dogs, with a reported incidence of 5–30%. Rates are lower in small dogs and higher in large breed dogs [9, 153–156]. Medical treatment is reported to successfully control the symptoms in 65–75% dogs [153, 157, 158].

Two retrospective reports, one of dogs with persistent urinary tract infections and one very large study of nearly 11 000 dogs with uroliths removed and submitted to a university laboratory for analysis, found spayed females to be at an increased risk for urinary tract infections compared with intact females [159, 160]. However, one casecontrol study of 78 dogs with naturally acquired urinary tract infections did not find such a relationship [161]. No association with urinary tract infections has been found for the neutering of male dogs [159]. The majority of uncomplicated urinary tract infections can be successfully resolved with antibiotic treatment.

Feline Lower Urinary Tract Disease (FLUTD) is a collection of symptoms ranging from mild haematuria and stranguria to potential life-threatening urinary tract obstruction [162]. Causes include idiopathic interstitial cystitis, urinary tract infection, urolithiasis and neoplasia [162]. FLUTD has been reported to occur in 1.3–4.6% cats in private practice and 7–8% cats in veterinary teaching hospitals [3, 163]. While some studies have found no association between FLUTD conditions and neutering [8, 164], and it does not appear that neutering affects the size of the urethra in male cats (a possible risk factor for obstruction) [165], several epidemiologic studies have found that neutering status does raise the risk of some causes of FLUTD [166, 167]. Castrated males were at an increased risk compared with intact males for all causes of FLUTD except for infection and urinary incontinence. Spayed females had an increased risk for urolithiasis, urinary tract infections and urinary tract tumours, but not other causes of FLUTD. Intact females had a decreased risk for most causes [167]. While most cases of FLUTD are treatable and not life-threatening, urinary tract obstruction in males is a very serious condition. This occurred in about 12% cats with FLUTD symptoms, and the risk is higher in castrated male cats [167, 168].

Hypothyroidism is usually due to autoimmune thyroiditis or idiopathic thyroid atrophy [169, 170]. It occurs in an estimated 0.2-0.3% dogs [171, 172]. An epidemiologic survey of 3206 dogs diagnosed with hypothyroidism at veterinary teaching hospitals, and a much smaller study of 66 dogs with hypothyroidism confirmed by thryotropin stimulation testing, both found that neutered dogs are at higher risk than intact dogs for developing hypothyroidism [171, 172]. However, one study of 136 dogs referred to a veterinary teaching hospital for suspected hypothyroidism found no difference in neuter status between those confirmed by thyrotropin stimulation testing to be hypothyroid and those in which the diagnoses was excluded [173]. Supplementation of thyroid hormone resolves the disease symptoms in most cases [172, 174].

Diabetes mellitus is a multifactorial disease that has a variety of manifestations and sequelae. Incidence in cats has been reported from 0.08 to 2%, with Burmese cats having a higher rate of occurrence than other breeds or mixed-breed cats [175–178]. Incidence in dogs is estimated at 0.19–0.64%, with significant breed variations [179, 180]. Diabetes is more common in male cats than females, and neutering is associated with an increased risk of diabetes in both male and female cats in some studies [176]. However, when age and weight are controlled for no effect of neutering is seen in other studies [178]. In dogs, diabetes is often reported to be more common in females than males [180, 181] though this is not found in all populations [177].

Castrated males were at a higher risk for diabetes than intact males in one study, though weight was not controlled for [182]. Some authors have suggested that intact females may be at a greater risk of diabetes because of the antagonistic effects of ovarian hormones on insulin, and spaying is an important part of regulating diabetes in female dogs [177]. Obesity is clearly a risk factor for diabetes in cats, though there is some debate about whether this is true in dogs, and since neutered animals are prone to be heavier than intact animals matched by breed and age, this may be a confounding factor creating the appearance of a direct effect of neutering on diabetes risk [175–177, 180, 181]. Diabetes is a serious chronic disease that can often be managed for long periods but cannot be cured.

Pancreatitis can manifest as a chronic or acute disease with varying degrees of severity and multifactorial causation [183]. The true incidence of pancreatitis is unknown, and although autopsy surveys have found evidence of inflammation in anywhere from less than 1% to more than 50% of dog pancreases, no study has reported the true incidence of clinical pancreatitis [184–186]. In dogs, there is some evidence that neutered animals may be at higher risk than intact animals for acute pancreatitis [187, 188].

Obesity is a common and growing clinical problem in dogs and cats. Though clear and consistent definitions do not exist, various reports have suggested that among dogs 18–44% are overweight and 2.9–7.6% are obese [189–191]. Among cats, an estimated 19–40% are overweight and 7.8% are obese [192–194]. Being overweight is a significant risk factor for many serious diseases [178, 195–197]. Almost all studies agree that neutered cats and dogs are more likely to be overweight or obese than intact cats and dogs [189–191, 193–195, 198–204]. However, the exact relationship between neutering and excess body weight has not been clearly established.

Some studies have indicated that neutered animals have a lower metabolic rate [205–208]. But other studies, which control for the proportion of lean body mass and fat in subjects, have found comparable metabolic rates in intact and neutered animals [202–204, 209]. There is evidence that neutered animals may gain excess weight because they eat more and expend less energy than intact animals despite having the same resting metabolic rate [83, 200, 204, 206, 207]. There are also many other risk factors for obesity, including sex, breed and variables associated with owners and their habits, that affect the chances of an animal becoming overweight regardless of whether it is neutered or intact [189, 194, 195, 210].

It is clear that obesity is preventable. Proper restriction of total calorie intake is all that is necessary to prevent obesity regardless of neuter status [189, 195].

Optimal Age for Neutering

For decades, the traditional age for neutering dogs and cats in the USA has been 6–9 months. There is no clear scientific basis for choosing this age, and it has been suggested that the practice arose as a response to anaesthetic mortality in younger animals in the first half of the twentieth century [8]. Anaesthetic procedures have evolved dramatically since that time, and it has since been demonstrated that not only is the procedure safe in puppies and kittens 7–12 weeks of age, but these younger patients actually recover faster and have fewer complications than those neutered at the traditional age [84, 103, 211].

One large-scale (775 cats and 1213 dogs) trial found no significant differences in the week immediately after surgery between cats and dogs neutered at the traditional age and earlier, apart from more minor surgical complications in the traditional age group [103]. Another study followed 31 kittens neutered at 7 weeks and at 7 months for 1 year and found no differences in any measures of behavioural or physical development [84]. Two large retrospective cohort studies followed puppies (n=269)and kittens (n=263) adopted from shelters and neutered before or after 24 weeks of age for approximately 3 years [212, 213]. Of the numerous measures of health, behaviour and relationship with owner examined in cats, the only difference detected was a greater incidence of urinary tract problems in the cats neutered at the traditional age [212]. In the canine study, puppies neutered earlier than 24 weeks did have a higher rate of infections, primarily parvovirus. This may have been due to differences in the management policies of the two shelters in which the subjects were neutered, since the rate of parvovirus infections was higher at the shelter where most of the early neutered animals were spayed or castrated [213]. Dogs in the traditional-neuter age group had more gastrointestinal problems than dogs in the early neutered group [213]. Interestingly, there was no difference in the incidence of urinary incontinence in female dogs in this study, which contrasts with an owner survey study of 206 dogs that found urinary incontinence occurred twice as often in females spayed after their first heat as those spayed before having a heat cycle [156].

A different group of researchers reported two very similar retrospective cohort studies following over 1800 dogs and 1600 cats adopted from shelters after being neutered (either before or after 5.5 months of age) for an average of 4-4.5 years, but as long as 11 years in some cases, and examined numerous behavioural and medical outcomes [9, 11]. For dogs, 7 out of 14 behavioural measures appeared affected by age at neutering, with early neutering worsening 3 problem behaviours and improving 4. Animals in the early neutered group exhibited higher rates of noise phobia and sexual behaviours. The early neutered group also exhibited less separation anxiety, fearful urination in the house and escaping. Early castrated males (but not spayed females) showed more aggression towards humans in the household and more barking. When only problems considered by owners to be serious were analysed, the reduced risk of escaping for the early neutered group was the only behaviour still significantly associated with age at neutering [9].

Of the medical conditions monitored, four were significantly associated with age at neutering. Dogs neutered early had higher rates of hip dysplasia, though the dysplasia seen in the traditional-age group was clinically worse and this group was far more likely to be euthanized for the problem than the early neutered group. Rates of cystitis and urinary incontinence were higher for females neutered before 5.5 months of age. The early neutered group had lower rates of respiratory infections but higher rates of parvoviral infection. And finally, the early Table 1 Effects of spaying on females. See text for more detail on incidence and clinical significance of specific conditions

Condition	How common?	How serious?	Effect of spaying	Species affected	Comments
Unwanted litters	Very common	Very	Prevents	Dog and cat	Significant pet overpopulation and associated euthanasia
Risks of reproduction	Uncommon	Variable	Prevents	Dog and cat	Dystocia, brucellosis, diabetes, others; risk of dystocia can be high for certain breeds
Mammary neoplasia Pyometra	Very common Very common	Very Very	↓Dramatically Prevents	Dog and cat Dog and cat	Generally poor prognosis
Uterine neoplasia	Rare	Variable	Prevents	Dog and cat	Some benign/removable, some
Otenne neoplasia	Nale	valiable	Flevenis	Doy and cat	malignant
Ovarian neoplasia Vaginal/Vulvar neoplasia	Uncommon Uncommon	Variable Moderate	Prevents ↓Dramatically	Dog and cat	mangham
dog Osteosarcoma	Uncommon	Very	Possibly ↑	Dog	Rare in most breeds, common in a few breeds
Haemangiosarcoma	Uncommon	Very	Î	Dog	Rare in most breeds, common in a few breeds
Transitional cell carcinoma	Uncommon	Very	↑	Dog	Incidence varies by breed
Cruciate ligament disease	Common	Moderate	\uparrow	Dog	Incidence varies by breed, surgically treatable
Hip dysplasia	Common	Variable	Probably ↑	Dog	Rare in most breeds, common in a few breeds
Aggressive behaviour	Common	Very	Possibly ↑	Dog and cat	
Urinary incontinence	Very common	Mild	↑ Î	Dog	Medically controllable in 65–75% of cases
Urinary tract infection	Common	Moderate	Possibly ↑	Dog	Easily treatable in most cases
Hypothyroidism	Uncommon	Moderate	Possibly ↑	Dog	Easily treatable
Diabetes mellitus	Uncommon	Very	Possibly ↑	Dog and cat	Incidence varies by breed
Acute pancreatitis	Uncommon	Very	Possibly ↑	Dog	
Obesity	Common	Very	Ť	Dog and cat	Easily prevented by calorie restriction
Longevity	-	-	Possibly ↑	Dog and cat	Spayed females may live longer than intact females

 \downarrow =decreases/reduces, \uparrow =increase/exacerbates.

neutered group had a lower rate of obesity than those dogs neutered at the traditional age. The remaining 43 outcome measures studied showed no difference between the two groups [9].

In the feline study, early neutering increased shyness around strangers for both sexes, and it increased hiding behaviour for males but not females. Early neutered cats showed less hyperactivity, and early neutered males showed less aggression towards veterinarians, less urine spraying and fewer sexual behaviours. There may also have been a decreased rate of scratching furniture in early neutered cats, but these cats were more likely to have been declawed, so the effect may be an artefact. When only problems considered serious were analysed, none of these behaviours was significantly associated with age at the neuter status [11].

Early neutered cats experienced lower rates of asthma and gingivitis, and males experienced fewer abscesses in the first 5–6 years after neutering. Cats neutered early may have experienced lower rates of cancer, but when only malignancies confirmed by a veterinarian were considered this effect was not significant. For the other 38 outcome measures studied, no difference between the groups was observed [11].

Considering the very large number of medical and behavioural conditions examined in the four retrospective studies of shelter animals, a few statistically significant associations were found. It is likely that with so many variables compared between groups some of these associations are spurious, and firm conclusions about a causal relationship between age at neuter and any given medical or behavioural conditions should not be made without a plausible biological mechanism and corroborating information from other studies. There were some differences in the specific associations identified by the two research groups. Despite similar methodologies and source populations, it is possible that these differences reflect true differences in the populations studied or the evaluation methods. However, if some of the associations identified are because of Type-I error, it would be expected that different studies would identify different spurious associations. Consistency between studies in identifying specific associations would strengthen the hypothesis that such associations are truly causal.

Table 2 Effects of castration on males. See text for more detail on incidence and clinical significance of specific conditions

Condition	How common?	How serious?	Effect of castration	Species affected	Comments
Unwanted litters	Very common	Very	Prevents	Dog and cat	Significant pet overpopulation and associated euthanasia
Testicular neoplasia Prostate disease	Uncommon Very common	Moderate Variable	Prevents ↓Dramatically	Dog Dog	Most benign and surgically removable Some have few symptoms others have severe, chronic disease
Behaviour problems	Common	Variable	Variable	Dog and cat	Conflicting studies; most report less aggression, roaming, urine marking
Perineal hernias Perianal fistulas	Uncommon Uncommon	Moderate Moderate	\downarrow	Dog Dog	Can often be repaired surgically Incidence varies by breed, some respond well to treatment others are serious chronic problem
Prostatic neoplasia Osteosarcoma	Uncommon Uncommon	Very Very	Probably ↑ Possibly ↑	Dog Dog	Poor prognosis Rare in most breeds, common in a few breeds
Haemangiosarcoma	Uncommon	Very	↑	Dog	Rare in most breeds, common in a few breeds
Cruciate ligament disease	Common	Moderate	Î	Dog	Incidence varies by breed, surgically treatable
Hip dysplasia	Common	Variable	Probably ↑	Dog	Rare in most breeds, common in a few breeds
Femoral physeal fracture	Uncommon	Moderate	Possibly ↑	Cat	Obesity may be confounding factor
Hypothyroidism Diabetes mellitus Acute pancreatitis	Uncommon Uncommon Uncommon	Moderate Very Very	Possibly ↑ Possibly ↑ Possibly ↑	Dog Dog and cat Dog	Easily treatable Incidence varies by breed
Obesity Longevity	Common –	Very _	↑ Possibly ↑	Dog and cat Dog and cat	Easily prevented by calorie restriction Castrated males may live longer than intact males

 \downarrow =decreases/reduces, \uparrow =increase/exacerbates.

Conclusions

It is apparent that spaying and castration have benefits for the pet population in general and both benefits and risks for individual dogs and cats. It is impossible to predict the precise outcome of neutering for any individual given the numerous and interacting aetiological factors involved in most serious behavioural and medical conditions. Any decision to neuter a particular pet must include consideration of individual circumstances and the values and goals of the owner as well as the risks and benefits identified by epidemiologic data. However, these research data do allow some cautious generalization about the magnitude and clinical importance of specific risks and benefits associated with neutering.

In females, spaying reduces or eliminates the risk of several common, serious disorders, including mammary neoplasia and pyometra, and eliminates the inconvenience and risk associated with oestrus and reproduction for both cats and dogs. It appears to increase the risk of a number of medical and behavioural conditions; however, many of these are either relatively uncommon or easily treated, and the absolute risk often varies markedly by breed. When the totality of the scientific evidence is considered, it appears justified to recommend spaying for most females not intended for breeding, because the procedure is more likely to prevent rather than cause disease. Table 1 summarizes the effects of spaying on females. Because the evidence is complex, such a shorthand summary can be a useful reference; however, it is necessarily an oversimplified representation that cannot convey the full complexity and ambiguity of the data.

In male dogs, the individual benefits of castration are not so clearly greater than the risks as they are for females. Males may be more likely to benefit than to be harmed by castration, but the balance of the evidence is close. The population benefits, of course, argue in favour of routine neutering of male dogs. For male cats, however, neutering confers more benefit than harm. Table 2 summarizes the effects of castration on males. Again, this is intended only as a convenient reference to the more detailed, nuanced information presented in the text.

The evidence is mixed regarding the risks and benefits of neutering dogs before 5–6 months of age, and so no strong recommendation for or against the practice can be made. The lack of clear and consistent associations between age at neutering and particular medical or behavioural outcomes despite several large studies suggests that there are unlikely to be many effects of great clinical significance for dogs or cats in general that are attributable to age at neutering. However, it is clear that spaying female dogs before their first heat is preferable to spaying them after this event, primarily because of the impact on the risk of mammary neoplasia.

There are many areas in which a greater quantity and quality of data would aid in evaluating the significance of specific risk and benefits associated with neutering. Establishing the true prevalence of many conditions potentially affected by neutering would be helpful in evaluating the importance of the effects of neutering on the relative risk of these conditions. Establishing that associations between neuter status and specific outcomes are truly causal, by confirming such associations in multiple studies of adequate size and quality, by investigating putative underling biologic mechanisms and by conducting experimental studies where feasible, would make it possible to know if these associations are truly relevant when making recommendations concerning neutering. And the clinical significance of these associations must be considered. Common and serious conditions prevented or caused by neutering clearly have more clinical importance than rare and minor or easily treated conditions. Finally, this information must be made available in a clear and accessible form to veterinarians and, through them, to pet owners.

It is critical to integrate relevant research evidence with the unique circumstances of each pet and owner when making recommendations concerning neutering. The evidence is complex and often inconclusive, so unambiguous predictions about outcomes for individual patients are rarely justified. There is, unfortunately, a tendency for lay people and veterinarians alike to react to the complexity and uncertainty of the research data by making broad generalizations or by sticking to habit and tradition. However, our pets are better served by a judicious and thoughtful evaluation of the quality and significance of existing and new data in the light of individual circumstances and the characteristics of each animal.

References

- Howe LM. Surgical methods of contraception and sterilization. Theriogenology 2006;66(3):500–9.
- 2. Kutzler M, Wood A. Non-surgical methods of contraception and sterilization. Theriogenology 2006;66(3):514–25.
- Lund EM, Armstrong PJ, Kirk CA, Kolar LM, Klausner JS. Health status and population characteristics of dogs and cats examined at private veterinary practices in the United States. Journal of the American Veterinary Medical Association 1999;214:1336–41.
- Poss JE, Bader JO. Attitudes toward companion animals among Hispanic residents of a Texas border community. Journal of Applied Animal Welfare Science 2007;10(3): 243–53.
- 5. Perrin T. The business of urban animals survey: The facts and statistics on companion animals in Canada. Canadian Veterinary Journal 2009;50:48–52.
- Blackshaw JK, Day C. Attitudes of dog owners to neutering pets: demographic data and effects of owner attitudes. Australian Veterinary Journal 1994;71(4):113–6.

- Spain CV, Scarlett JM, Cully SM. When to neuter dogs and cats: a survey of New York state veterinarians' practices and beliefs. Journal of the American Animal Hospital Association 2002;38(5):482–8.
- Root Kustritz MV. Determining the optimal age for gonadectomy of dogs and cats. Journal of the American Veterinary Medical Association 2007;231(11):1665–75.
- Spain CV, Scarlett JM, Houpt KA. Long-term risks and benefits of early-age gonadectomy in dogs. Journal of the American Veterinary Medical Association 2004;224(3):380–7.
- Reichler IM. Gonadectomy in cats and dogs: a review of the risks and benefits. Reproduction in Domestic Animals 2009;44(2, Suppl.):29–35.
- Spain CV, Scarlett JM, Houpt KA. Long-term risks and benefits of early-age gonadectomy in cats. Journal of the American Veterinary Medical Association 2004;224(3):372–9.
- Zink C. Early spay-neuter considerations for the canine athlete: one veterinarian's opinion; 2005. Available from: URL: http://www.caninesports.com/SpayNeuter.html (accessed 12 February 2009).
- Howe LM. Rebuttal to "Early spay-neuter considerations for the canine athlete"; 2005. Available from: URL: http:// www.columbusdogconnection.com/Documents/ PedRebuttal%20.pdf (accessed 12 February 2009).
- Sanborn LJ. The long-term health effects of spay/neuter in dogs; 2007. Available from: URL: http://www.naiaonline.org/ pdfs/LongTermHealthEffectsOfSpayNeuterInDogs.pdf (accessed 12 February 2009).
- Orzeszko G, Orzeszko K. Should I spay or should I no? The pros and cons of neutering; 2007. Available from: URL: http://users.lavalink.com.au/theos/Spay-neuter.htm (accessed 12 February 2009).
- Cockcroft PD, Holmes MA. Handbook of Evidence-Based Veterinary Medicine. Blackwell Publishing, Oxford, UK; 2003.
- Trevejo RT. A small animal clinician's guide to critical appraisal of the evidence in scientific literature. Veterinary Clinics of North America: Small Animal Practice 2007;37(3):463–75.
- Schwarz LM, Woloshin S, Dvorin EL, Welch HG. Ratio measures in leading medical journals: structured review of accessibility of underlying absolute risks. British Medical Journal 2006;333(7581):1248.
- Vandenbrouke JP, von Elm E, Altman DG, Gøtzsche PC, Mulrow CD, Pocock SJ, *et al.* Strengthening the reporting of observational studies in epidemiology (STROBE): explanation and elaboration. Epidemiology 2007;18(6):805–35.
- Clancy EA, Rowan AN. companion animal demographics in the United States: a historical perspective. In: Salem DJ, Rowan AN, editors. The State of the Animals II. Humane Society Press, Washington, DC; 2003. p. 9–26.
- Olson PN, Moulson C. Pet (dog and cat) overpopulation in the United States. Journal of Reproduction and Fertility 1993;47(Suppl.):433–8.
- Mahlow JC. Estimation of the proportions of dogs and cats that are surgically sterilized. Journal of the American Veterinary Medical Association 1999;215(5):640–3.
- 23. New JC. Characteristics of shelter-relinquished animals and their owners compared with animals and their owners in

U.S. pet-owning households. Journal of Applied Animal Welfare Science 2000;3(3):179–201.

- Patronek GJ, Glickman LT, Beck AM, McCabe GP, Ecker C. Risk factors for relinquishment of dogs to an animal shelter. Journal of the American Veterinary Medical Association 1996;209(3):572–81.
- Zawistowski S, Morris J, Salman MD, Ruch-Gallie R. Population dynamics, overpopulation, and the welfare of companion animals: new insights on old and new data. Journal of Applied Animal Welfare Science 1998;1(3):193–206.
- Salman MD, New JG, Scarlett JM, Kris PH. Human and animal factors related to the relinquishment of dogs and cats in 12 selected animal shelter I the United States. Journal of Applied Animal Welfare 1998;1(3):207–26.
- Jessup DA. The welfare of feral cats and wildlife. Journal of the American Veterinary Medical Association 2004;225(9):1377–83.
- Slater MR. Understanding issues and solutions for unowned, free-roaming cat populations. Journal of the American Veterinary Medical Association 2004;225(9):1350–4.
- Levy JK. Humane strategies for controlling feral cat populations. Journal of the American Veterinary Medical Association 2004;225(9):1354–60.
- Stoskopf MK. Analyzing approaches to feral cat management-one size does not fit all. Journal of the American Veterinary Medical Association 2004;225(9):1361–64.
- Carmichael LE, Greene CE. Canine brucellosis. In: Greene CE. Infectious Diseases of the Dog and Cat, 3rd edn. WB Saunders, Philadelphia, PA; 2006. p. 369–81.
- Nassar R, Mosier JE. Feline population dynamics: a study of the Manhattan, Kansas, feline population. American Journal of Veterinary Research 2001;43(1):167–70.
- Budke CM, Slater MR. Utilization of matrix population models to assess a 3-year single treatment nonsurgical contraception program versus surgical sterilization in feral cat populations. Journal of Applied Animal Welfare Science 2009;12(4):277–92.
- World Organization for Animal Health (OIE). Guidelines on stray dog population control. Chapter 7.7 of Terrestrial Health Code 2009. Available from: URL: http://www.oie.int/eng/ normes/mcode/en_chapitre_1.7.7.htm (accessed 3 October 2010).
- Reece JF, Chawla SK. Control of rabies in Jaipur, India, by the sterilization and vaccination of neighborhood dogs. Veterinary Record 2006;159(12):379–83.
- Rupprecht CE, Hanlon CA, Slate D. Control and prevention of rabies in animals: paradigm shifts. Developments in Biologicals 2006;125:103–11.
- Amaku M, Augusto Dias R, Ferreira F. Canine population dynamics: potential effects of sterilization campaigns. Revista Panamericana de Salud Pulblica 2009;25(4):300–4.
- Panda AK, Thakur SD, Katoch RC. Rabies: control strategies for the Himalayan states of the Indian subcontinent. Journal of Communicable Diseases 2008;40(3):169–75.
- Imnadze P, Surguladze V, Tushishvili T, Baidoshvili L. Rabies control and prevention in Georgia: current status and perspectives. Developments in Biologicals 2008;131:387–91.

- Forsberg CL, Persson G. A survey of dystocia in the Boxer breed. Acta Veterinaria Scandinavica 2007;21:49–58.
- Bergstrom A, Nødtvedt A, Lagerstedt AS, Egenvall A. Incidence and breed predilection for dystocia and risk factors for cesarean section in a Swedish population of insured dogs. Veterinary Surgery 2006;35(8):786–91.
- Gunn-Moore DA, Thrushfield MV. Feline dystocia: prevalence and association with cranial conformation and breed. Veterinary Record 1995;136(14):350–3.
- Johnston SD, Root Kustritz MV, Olson PNS. Canine and Feline Theriogenology. WB Saunders, Philadelphia, PA; 2001. p. 80–7.
- 44. Lana SE, Rutteman GR, Winthrow SJ. Tumors of the mammary gland. In: Winthrow SJ, Vail DM, editors. Withrow and MacEwen's Small Animal Clinical Oncology, 4th edn. WB Saunders Elsevier, St. Louis, MO; 2007. p. 619–36.
- Moe L. Population-based incidence of mammary tumors in some dog breeds. Journal of Reproduction and Fertility 2001;57:439–43.
- Dobson JM, Samuel S, Milstein H, Rogers K, Wood JL. Canine neoplasia in the UK: estimates of incidence from a population of insured dogs. Journal of Small Animal Practice 2002;43(6):240–6.
- Egenvall A, Bonnett BN, Ohagen P, Olson P, Hedhammar A, von Euler H. Incidence of and survival after mammary tumors in a population of over 80,000 insured female dogs in Sweden from 1995 to 2002. Preventative Veterinary Medicine 2002;69:109–27.
- Overly B, Shofer FS, Goldschmidt MH, Sherer D, Sorenmo KU. Association between ovariohysterectomy and feline mammary carcinoma. Journal of Veterinary Internal Medicine 2005;19(4):560–3.
- Hayes HM Jr., Milne KL, Mandell CD. Epidemiologic features of feline mammary carcinoma. Veterinary Record 1981;108(22):476–9.
- Sorenmo KU, Shofer FS, Goldschmidt MH. Effect of spaying and timing of spaying on survival of dogs with mammary carcinoma. Journal of Veterinary Internal Medicine 2000;14:266–70.
- Schneider R, Dorn CR, Taylor DO. Factors influencing canine mammary cancer development and postsurgical survival. Journal of the National Cancer Institute 1969;43:1249–61.
- Nelson RW, Feldman EC, Stabenfeldt GH. Treatment of canine pyometra and endometritis with prostaglandin F2alpha. Journal of the American Veterinary Medical Association 1982;181:899–903.
- Myers-Wallen VN, Goldschmidt MH, Flickinger GL. Prostaglandin F2alpha treatment of canine pyometra. Journal of the American Veterinary Medical Association 1986;189:1557–61.
- 54. Gilbert RO, Nöthling JO, Oettle EE. A retrospective study of 40 cases of canine pyometra-metritis treated with prostaglandin F-2 alpha and broad-spectrum antibacterial drugs. Journal of Reproduction and Fertility Supplement 1989;39:225–9.
- Rootwelt-Andersen V, Farstad W. Treatment of pyometra in the bitch: A survey among Norwegian small animal practitioners. European Journal of Companion Animal Practice 2006;16(2):195–8.

- Trasch K, Wehrend A, Bostedt H. Follow-up examinations of bitches after conservative treatment of pyometra with the antigestagen aglepristone. Journal of Veterinary Medicine. A, Physiology, Pathology, Clinical Medicine 2003;50(7):375–9.
- Gürbulak K, Pancarci M, Ekici H, Konuk C, Kirşan I, *et al.* Use of aglepristone and aglepristone + intrauterine antibiotic for the treatment of pyometra in bitches. Acta Veterinaria Hungarica 2005;53(2):249–55.
- England GC, Freeman SL, Russo M. Treatment of spontaneous pyometra in 22 bitches with a combination of cabergoline and cloprosteenol. Veterinary Record 2007;160(9):293–96.
- Egenvall A, Hagman R, Bonnett BN, Hedhammar A, Olson P, Lagerstedt AS. Breed risk of pyometra in insured dogs in Sweden. Journal of Veterinary Internal Medicine 2001;15:530–8.
- van Goethem B. Making a rational choice between ovariectomy and ovariohysterectomy in the dog: a discussion of the benefits of either technique. Veterinary Surgery 2006;35(2):136–43.
- Klein, MK. Tumors of the female reproductive system. In: Winthrow SJ, Vail DM, editors. Withrow and MacEwen's Small Animal Clinical Oncology, 4th edn. WB Saunders Elsevier, St. Louis, MO; 2007. p. 610–8.
- Millan Y, Gordon A, Espinosa de los Monteros A, Reymundo C, Martin de las Mulas J. Steroid receptors in canine and human female genital tract tumours with smooth muscle differentiation. Journal of Comparative Pathology 2007;136:197–201.
- Brodey RS, Roszel JF. Neoplasms of the canine uterus, vagina, and vulva: a clinicopathologic survey of 90 cases. Journal of the American Veterinary Medical Association 1967;151:1294–307.
- Thatcher C, Bradley RL. Vulvar and vaginal tumors in the dog – a retrospective study. Journal of the American Veterinary Medical Association 1983;183:690–2.
- Grieco, V, Riccardi E, Greppi GF, Teruzzi F, Iermanò V, Finazzi M. Canine testicular tumours: a study on 232 dogs. Journal of Comparative Pathology 2008;138:86–9.
- Hayes Jr H, Pendergrass T. Canine testicular tumors: epidemiologic features of 410 dogs. International Journal of Cancer 1976;18:482–7.
- 67. Fan TM, de Lorimier L. Tumors of the male reproductive system. In: Winthrow SJ, Vail DM, editors. Withrow and MacEwen's Small Animal Clinical Oncology, 4th edn.WB Saunders Elsevier, St. Louis, MO; 2007. p. 637–48.
- Liao AT, Chu PY, Yeh LS, Lin CT, Liu CH. A 12-year retrospective study of canine testicular tumors. Journal of Veterinary Medical Science 2009;71(7):919–23.
- Mukaratirwa S, Chitura T. Canine subclinical prostatic disease: histologic prevalence and validity of digital rectal examination as a screening test. Journal of the South African Veterinary Association 2007;78(2):66–8.
- Berry SJ, Strandberg JD, Saunders WJ, Coffey DS. Development of canine benign prostatic hyperplasia with age. Prostate 1986;9(4):363–73.
- Lowseth LA, Gerlach RF, Gillett NA, Muggenburg BA. Age-related changes in the prostate of the beagle dog. Veterinary Patology 1990;27:347–53.

- Teske E, Naan EC, van Dijk EM, Van Garderen E, Schalken JA. Canine prostate carcinoma: epidemiological evidence of an increased risk in castrated dogs. Molecular and Cellular Endocrinology 2002;197(1–2):251–5.
- Scarlett JM, Salman MD, New JG, Kass PH. The role of veterinary practitioners in reducing dog and cat relinquishments and euthanasias. Journal of the American Veterinary Medical Association 2002;220(3):306–11.
- Overall KL. Clinical Behavioral Medicine for Small Animals. Mosby, St. Louis, MO; 1997.
- Borchelt PL. Aggressive behavior of dogs kept as companion animals: classification and influence of sex, reproductive status, and breed. Applied Animal Ethology 1983;10:45–61.
- Write JC, Nesselrote MS. Classification of behavioral problems in dogs: distributions of age, breed, sex, and reproductive status. Applied Animal Behavior Science 1987;19:169–78.
- Gershman KA, Sacks JJ, Wright JC. Which dogs bite? A case-control study of risk factors. Pediatrics 1994; 93(6 Pt 1):913–7.
- Hopkins SG, Schubert TA, Hart BL. Castration of adult male dogs: effects on roaming, aggression urine spraying, and mounting. Journal of the American Veterinary Medical Association 1976;168:1108–10.
- Maarschalkerweerd RJ, Endenburg N, Kirpensteijn J, Knol BW. Influence of orchiectomy on canine behaviour. Veterinary Record 1997;140(24):617–69.
- Neilson JC, Eckstein RA, Hart BL. Effects of castration on problem behaviors in male dogs with reference to age and duration of behavior. Journal of the American Veterinary Medical Association 1997;211(2):180–2.
- Knol BW, Egberink-Alink ST. Treatment of problem behaviour in dogs and cats by castration and progestagen administration: a review. Veterinary Quarterly 1989;11(2):102–7.
- Hart BL, Cooper LC. Factors relating to urine spraying and fighting in prepubertally gonadectomized cats. Journal of the American Veterinary Medical Association 1984;184(10):1255–8.
- Hart BL, Barrrett RE. Effects of castration on fighting, roaming, and urine spraying in adult male cats. Journal of the American Veterinary Medical Association 1973;163:290–2.
- Stubbs WP, Bloomberg MS, Scruggs SL, Shille VM, Lane TJ. Effects of prepubertal gonadectomy on physical and behavioral development in cats. Journal of the American Veterinary Medical Association 1996;209(11):1864–71.
- Niebauer GW, Shibly S, Seltenhammer M, Pirker A, Brandt S. Relaxin of prostatic origin might be linked to perineal hernia formation in dogs. Annals of the New York Academy of Sciences 2005;1041(0):415–22.
- Maute AM, Koch DA, Montavon PM. Perineale Hernie beim Hund – Colopexie, Vasopexie, Cystopexie und Kastration als Therapie der Wahl bei 32 Hunden. [Perineal hernia in dogs – colopexy, vasopexy, cystopexy and castration as an alternative therapy in 32 dogs]. Schweizer Archiv Fur Tierheilkunde 2001;143(7):360–7.
- Hayes HM. The epidemiologic features of perineal hernia in 771 dogs. Journal of the American Animal Hospital Association 1978;14:703–12.

- Sjollema BE, van Sluijs FJ. Perineal hernia in the dog: developments in its treatment and retrospective study in 197 patients. Tijdschrift voor Diergeneeskunde 1991;116(3):142–7 (in Dutch).
- Killingsworth CR, Walshaw R, Dunstan RW, Rosser Jr EJ. Bacterial population and histologic changes in dogs with perianal fistula. American Journal of Veterinary Research 1988;49(10):1736–41.
- Stanley BJ, Hauptman JG. Long-term prospective evaluation of topically applied 0.1% tacrolimus ointment for treatment of perianal sinuses in dogs. Journal of the American Veterinary Medical Association 2009;235(4):397–404.
- Lombardi RL, Marino DJ. Long-term evaluation of canine perianal fistula disease treated with exclusive fish and potato diet and surgical excision. Journal of the American Veterinary Medical Association 2008;44(6):302–7.
- Zoran DL. Rectoanal disease. In: Ettinger SJ, Feldman EC, editors. Textbook of Veterinary Internal Medicine, 6th edn. Elsevier, St. Louis, MO: 2005. p. 1408–20.
- Michell AR. Longevity of British breeds of dog and its relationship with sex, size, cardiovascular variables, and disease. Veterinary Record 1999;145(22):625–9.
- Bronson RT. Variation in age at death of dogs of different sexes and breeds. American Journal of Veterinary Research 1982;43(11):2057–9.
- Moore GE, Burkman KD, Carter MN, Peterson MR. Causes of death or reasons for euthanasia in military working dogs: 927 cases (1993–1996). Journal of the American Veterinary Medical Association 2001;219(2):209–14.
- Drori D, Folman Y. Environmental effects on longevity in the male rat: exercise, mating, castration and restricted feeding. Experimental Gerontology 1976;11(1–2):25–32.
- 97. Waters DJ, Shen S, Glickman LT. Life expectancy, antagonistic pleiotropy, and the testis of dogs and men. Prostate 2000;43(4);272–7.
- Kraft W. Geriatrics in canine and feline internal medicine. European Journal of Medical Research 1998;3:3–41.
- Greer KA, Canterberry SC, Murphy KE. Statistical analysis regarding the effects of height and weight on life span of the domestic dog. Research in Veterinary Science 2007;82:208–14.
- Waters DJ, Kengeri SS, Clever B, Booth JA, Maras AH, Schlittler DL, et al. Exploring mechanisms of sex differences in longevity: lifetime ovary exposure and exceptional longevity in dogs. Aging Cell 2009;8(6):752–5.
- Cooley DM, Beranek BC, Schlittler DL, Glickman NW, Glickman LT, Waters DJ. Endogenous gonadal hormone exposure and bone sarcoma risk. Cancer Epidemiology, Biomarkers, and Prevention 2002;11:1434–40.
- 102. Pollari FL, Bonnett BN, Bamsey SC, Meek AH, Allen DG. Postoperative complications of elective surgeries in dogs and cats determined by examining electronic and paper medical records. Journal of the American Veterinary Medical Association 1996;208(11):1882–6.
- Howe LM. Short-term results and complications of prepubertal gonadectomy in cats and dogs. Journal of the American Veterinary Medical Association 1997;211(1):57–62.
- 104. Pollari FL, Bonnettt BN. Evaluation of postoperative complications following elective surgeries of dogs and cats

at private practices using computer records. Canadian Veterinary Journal 1996;37:672–8.

- Burrow R, Batchelor D, Cripps P. Complications observed during and after ovariohysterectomy of 142 bitches at a veterinary teaching hospital. Veterinary Record 2005;157(26):829–33.
- 106. Cornell KK, Bostwick DG, Cooley DM, Hall G, Harvey HJ, Hendrick MJ, *et al.* Clinical and pathologic aspects of spontaneous canine prostate carcinoma: a retrospective analysis of 76 cases. Prostate 2000;45(2):173–83.
- O'Shea JP. Studies on the canine prostate gland II: prostatic neoplasms. Journal of Comparative Pathology 1963;73:244–52.
- 108. Leav I, Ling GV. Adenocarcinoma of the canine prostate gland. Cancer 1968;22:1329–45.
- Obradovich J, Walshaw BVMS, Goullaud E. The influence of castration on the development of prostatic carcinoma in the dog: 43 cases (1978–1985). Journal of Veterinary Internal Medicine 1987;1(4):183–7.
- Sorenmo KU, Goldschmidt M, Shofer F, Goldkamp C, Ferracone J. Immunohistochemical characterization of canine prostatic carcinoma and correlation with castration status and castration time. Veterinary Comparative Oncology 2003;1(1):48–56.
- Ru G, Terracini B, Glickman LT. Host related risk factors for canine osteosarcoma. Veterinary Journal 1998;156(1):31–9.
- Dernall WS. Tumors of the skeletal system. In: Winthrow SJ, Vail DM, editors. Withrow and MacEwen's Small Animal Clinical Oncology, 4th edn. WB Saunders Elsevier, St. Louis, MO; 2007. p. 540–82.
- Rosenberger JA, Pablo NV, Crawford PC. Prevalence of intrinsic risk factors for appendicular osteosarcoma in dogs: 179 cases (1996–2005). Journal of the American Veterinary Medical Association 2007;231(7):1076–80.
- Thamm, D. Hemangiosarcoma. In: Winthrow SJ, Vail DM, editors. Withrow and MacEwen's Small Animal Clinical Oncology. 4th edn. WB Saunders Elsevier, St. Louis, MO; 2007. p. 785–794.
- 115. Prymak C, McKee LJ, Goldschmidt MH, Glickman LT. Epidemiologic, clinical, pathologic, and prognostic characteristics of splenic hemangiosarcoma and splenic hematoma in dogs: 217 cases (1985). Journal of the American Veterinary Medical Association 1988; 193(6):706–12.
- Smith AN. Hemangiosarcoma in dogs and cats. Veterinary Clinics of North America: Small Animal Practice 2003;33:533–52.
- 117. Ware WA, Hopper DL. Cardiac tumors in dogs: 1982–1995. Journal of Veterinary Internal Medicine 1999;13:95–103.
- Knapp DW. Tumors of the urinary system. In: Winthrow SJ, Vail DM, editors. Withrow and MacEwen's Small Animal Clinical Oncology, 4th edn. WB Saunders Elsevier, St. Louis, MO; 2007. p. 649–58.
- Norris AM, Laing EJ, Valli VE, Withrow SJ, Macy DW, Ogilvie GK, *et al.* Canine bladder and urethral tumors: A retrospective study of 115 cases (1980–1985). Journal of Veterinary Internal Medicine 1992;6(3):145–53.

- Knapp DW, Glickman NW, DeNicola DB, Glickman LT. Naturally-occurring transitional cell carcinoma of the urinary bladder. Urologic Oncology 2000;5:47–59.
- Whitehair JG, Vasseur PB, Willits NH. Epidemiology of cranial cruciate ligament rupture in dogs. Journal of the American Veterinary Medical Association 1993;203(7):1016–9.
- 122. Duval JM, Budsberg SC, Flo GL, Sammarco JL. Breed, sex, and body weight as risk factors for rupture of the cranial cruciate ligament in young dogs. Journal of the American Veterinary Medical Association 1999;215(6):811–4.
- 123. Slauterbeck JR, Pankratz K, Xu KT, Bozeman SC, Hardy DM. Canine ovariohysterectomy and orchiectomy increases the prevalence of ACL injury. Clinical Orthopaedics and Related Research 2004;429:301–5.
- 124. Witsberger TH, Villamil JA, Schultz LG, Hahn AW, Cook JL. Prevalence of and risk factors for hip dysplasia and cranial cruciate ligament deficiency in dogs. Journal of the American Veterinary Medical Association 2008;232(12):1818–24.
- 125. Duerr FM, Duncan CG, Savicky RS, Park RD, Egger EL, Palmer RH. Risk factors for excessive tibial plateau angle in large breed dogs with cranial cruciate ligament disease. Journal of the American Veterinary Medical Association 2007;231(11):1688–91.
- Aragon CL, Budsberg SC. Applications of evidence-based medicine: cranial cruciate ligaments injury repair in the dog. Veterinary Surgery 2005;34(2):93–8.
- 127. Canapp SO. The canine stifle. Clinical Techniques in Small Animal Practice 2007;22(4):195–205.
- 128. Genevois JP, Remy D, Viguier E, Carozzo C, Collard F, Cachon T, *et al.* Prevalence of hip dysplasia according to official radiographic screening among 31 breeds of dogs in France. Veterinary and Comparative Orthopaedics and Traumatology 2008;21(1):21–4.
- 129. Paster ER, LaFond E, Biery DN, Iriye A, Gregor TP, Shofer FS, et al. Estimates of prevalence of hip dysplasia in Golden Retrievers and Rottweilers and the influence of bias on published prevalence figures. Journal of the American Veterinary Medical Association 2005;226(3):387–92.
- 130. Smith GK, Popovitch CA, Gregor TP, Shofer FS. Evaluation of risk factors for degenerative joint disease associated with hip dysplasia in German Shepherd Dogs, Golden Retrievers, Labrador Retrievers, and Rottweilers. Journal of the American Veterinary Medical Association 2001;219(12):1719–24.
- Jessen, CR. Spurrell, FA. Heritability of canine hip dysplasia. In: Proceedings Canine Hip Dysplasia Symposium, 19–20 October 1972, St. Louis, MO, USA; 1972. p. 53–61.
- 132. Hedhammar A, Olsson SE, Andersson SA, Persson L, Pettersson L, Olausson A, *et al.* Canine hip dysplasia: a study of heritability in 401 litters of German shepherd dogs. Journal of the American Veterinary Medical Association 1979;174:1012–6.
- 133. van Hagen MA, Ducro BJ, van den Broek J, Knol BW. Incidence, risk factors, and heritability estimates of hind limb lameness caused by hip dysplasia in a birth cohort of boxers. American Journal of Veterinary research 2005;66(2):307–12.
- 134. Vezzoni A, Dravelli G, Vezzoni L, De Lorenzi M, Corbari A, Cirla A, *et al.* Comparison of conservative management and juvenile pubic symphysiodesis in the early treatment

of canine hip dysplasia. Veterinary and Comparative Orthopaedics and Traumatology 2008;21(3):267–79.

- 135. Manley PA, Adams WM, Danielson KC, Dueland RT, Linn KA. Long-term outcome of juvenile pubic symphysiodesis and triple pelvic osteotomy in dogs with hip dysplasia. Journal of the American Veterinary Medical Association 2007;230(2):206–10.
- Impellizeria JA, Tetrick MA, Muir P. Effect of weight reduction on clinical signs of lameness in dogs with hip osteoarthritis. Journal of the American Veterinary Medical Association 2000;216:1089–91.
- Skurla CT, Egger EL, Schwarz PD, James SP. Owner assessment of the outcome of total hip arthroplasty in dogs. Journal of the American Veterinary Medical Association 2000;217(7):1010–2.
- 138. Remedios AM, Fries CL. Treatment of canine hip dysplasia: a review. Canine Veterinary Journal 1995;36(8):503–9.
- Leighton EA. Genetics of canine hip dysplasia. Journal of the American Veterinary Medical Association 1997;210(10):1474–9.
- 140. Ginja MM, Silvestre AM, Gonzalo-Orden JM, Ferreira AJ. Diagnosis, genetic control and preventive management of canine hip dysplasia: a review. Veterinary Journal 2010;184(3):269–76.
- Harasen G. Atraumatic proximal femoral physeal fractures in cats. Canadian Veterinary Journal 2004;45(4):359–60.
- 142. Craig LE. Physeal dysplasia with slipped capital femoral epiphysis in 13 cats. Veterinary Pathology 2001;38:92–7.
- 143. McNicholas WT, Wilkens BE, Blevins WE, Snyder PW, McCabe GP, Applewhite AA *et al.* Spontaneous femoral capital physeal fractures in adult cats: 26 cases (1996–2001). Journal of the American Veterinary Medical Association 2002;221(12):1731–6.
- 144. Fischer HR, Norton J, Kobluk CN, Reed AL, Rooks RL, Borostyankoi F. Surgical reduction and stabilization for repair of femoral capital physeal fractures in cats: 13 cases (1998–2002). Journal of the American Veterinary Medical Association 2004;224(9):1478–82.
- 145. Root MV, Johnston SD, Olson PN. The effect of prepuberal and postpuberal gonadectomy on radial physeal closure in male and female domestic cats. Veterinary Radiology and Ultrasound 1997;38:42–7.
- 146. Duffy DL, Serpell JA. Non-reproductive effects of spaying and neutering on behavior in dogs. In: Proceedings of the 3rd International Symposium on Non-Surgical Contraceptive Methods for Pet Population Control, 9–12 November 2006, Alexandria, VA, USA; 2006. Available from: URL: http://www.acc-d.org/2006%20Symposium%20Docs/ Duffy2.pdf
- 147. O'Farrell V, Peachy E. Behavioural effects of ovariohysterectomy on bitches. Journal of Small Animal Practice 1990;31:595–8.
- Reisner IR, Houpt KA, Shofer FS. National survey of owner-directed aggression in English Springer Spaniels. Journal of the American Veterinary Medical Association 2005;227(10):1594–603.
- 149. Kim HH, Yeon SC, Houpt KA, Lee HC, Chang HH, Lee HJ. Effects of ovariohysterectomy on reactivity in German Shepherd dogs. Veterinary Journal 2006;172(1):154–9.

- 150. Salmeri KR, Bloomberg MS, Scruggs SL, Shille V. Gonadectomy in immature dogs: effects on skeletal, physical, and behavioral development. Journal of the American Veterinary Medical Association 1991;198(7):1193–203.
- 151. Hart BL. Effect of gonadectomy on subsequent development of age-related cognitive impairment in dogs. Journal of the American Veterinary Medical Association 2001;219(1):51–6.
- 152. Neilson JC, Hart BL, Cliff KD. Prevalence of behavioral changes associated with age-related cognitive impairment in dogs. Journal of the American Veterinary Medical Association 2001;218:1787–91.
- 153. Angiolettti A, De Francesco I, Vergottini M, Battocchio ML. Urinary incontinence after spaying in the bitch: incidence and oestrogen therapy. Veterinary Research Communication 2004;28(Suppl. 1):153–5.
- Okkens AC, Kooistra HS, Nickel RF. Comparison of long-term effects of ovariectomy versus ovariohysterectomy in bitches. Journal of Reproduction and Fertility 1997;51:227–31.
- 155. Arnold S. Hanrinkontinenz bei kastrierten Hundinnen. Teil 1: Bedeutung, Klinik und Atiopathogenese [Urinary incontinence in castrated bitches. Part 1: Significance, clinical aspects, and etiopathogenesis]. Schweizer Archiv Fur Tierheilkunde 1997;139(6):271–6.
- Stocklin-Gautschi NM, Hässig M, Reichler IM, Hubler M, Arnold S. The relationship of urinary incontinence to early spaying in bitches. Journal of Reproduction and Fertility 2001;57(Suppl.):233–6.
- 157. Byron JK, March PA, Chew DJ, DiBartola SP. Effect of phenylpropanolamine and pseudoephedrine on the urethral pressure profile and continence scores of incontinent female dogs. Journal of Veterinary Internal Medicine 2007;21(1):47–53.
- 158. Nendick PA, Clark WT. Medical therapy of urinary incontinence in ovariectomised bitches: a comparison of the effectiveness of Diethylstilboestrol and Pseudoephedrin. Australian Veterinary Journal 1987;64(4):117–8.
- Seguin MA, Vaden SL, Altier C, Stone E, Levine JF. Persistent urinary tract infections and reinfections in 100 dogs (1989–1999). Journal of Veterinary Internal 2003;17:622–31.
- Ling GV, Franti CE, Johnson DL, Ruby AL. Urolithiasis in dogs III: prevalence of urinary tract infection and interrelations of infections, age, sex, and mineral composition. American Journal of Veterinary Research 1998;59(5):643–9.
- Freshman, JL, Reif JS, Allen TA, Jones, RL. Risk factors associated with urinary tract infection in female dogs. Preventative Veterinary Medicine 1989;7:59–67.
- Hostutler RA, Chew DJ, DiBartola SP. Recent concepts in feline lower urinary tract disease. Veterinary Clinics of North America: Small Animal Practice 2005;35:147–70.
- Forrester SD, Roudebush P. Evidence-based management of feline lower urinary tract disease. Veterinary Clinics of North America: Small Animal Practice 2007;37(3):533–58.
- 164. Buffington CA, Westropp JL, Chew DJ, Bolus RR. Risk factors associated with clinical signs of lower urinary tract disease in indoor-housed cats. Journal of the American Veterinary Medical Association 2006;228(5):722–5.

- 165. Root MV, Johnston SD, Johnston GR, Olson PN. The effect of prepuberal and postpuberal gonadectomy on penile extrusion and urethral diameter in the domestic cat. Veterinary Radiology 1996;37(5):363–8.
- Willeberg P, Priester WA. Feline urological syndrome: association with some time, space, and individual patient factors. American Journal of Veterinary Research 1976;37:975–8.
- Lekcharoensuk C, Osborne CA, Lulich JP. Epidemiologic study of risk factors for lower urinary tract disease in cats. Journal of the American Veterinary Medical Association 2001;218(9):1429–35.
- Roen DT. Questions interaction of sex and age on the risk of lower urinary tract disease in cats. Journal of the American Veterinary Medical Association 2001;219(2):173–4.
- Kemppainen RJ, Clark TP. Etiopathogenesis of canine hypothyroidism. Veterinary Clinics of North America: Small Animal Practice 1994;24(3):467–76.
- Graham PA, Refsal KR, Nachreiner RF. Etiopathologic findings of canine hypothyroidism. Veterinary Clinics of North America: Small Animal Practice 2007;37(4):617–31.
- Milne KL, Hayes HM. Epidemiologic features of canine hypothyroidism. Cornell Veterinarian 1981;71(1):3–14.
- Panciera DL. Hypothyroidism in dogs: 66 cases (1987–1992). Journal of the American Veterinary Medical Association 1994;204(5):761–7.
- Dixon RM, Reid SW, Mooney CT. Epidemiological, clinical, haematological and biochemical characteristics of canine hypothyroidism. Veterinary Record 1999;145(17):481–7.
- Scott-Moncrieff JCR, Guptill-Yoran L, Hypothyroidism. In: Ettinger SJ, Feldman EC, editors. Textbook of Veterinary Internal Medicine, 6th edn. Elsevier, St. Louis, MO; 2005. p. 1535–44.
- 175. McCann TM, Simpson KE, Shaw DJ, Butt JA, Gunn-Moore DA. Feline diabetes mellitus in the UK: the prevalence within an insured cat population and a questionnaire-based putative risk factor analysis. Journal of Feline Medicine and Surgery 2007;9(4):289–99.
- 176. Panciera DL, Thomas CB, Eicker SW, Atkins CE. Epizootiologic patterns of diabetes mellitus in cats: 333 cases (1980–1986). Journal of the American Veterinary Medical Association 1990;197(11):1504–8.
- 177. Rand JS, Fleeman LM, Farrow HA, Appleton DJ, Lederer R. Canine and feline diabetes mellitus: Nature or nurture? The Journal of Nutrition 2004;134:2072S–80S.
- 178. Prahl A, Guptill L, Glickman NW, Tetrick M, Glickman LT. Time trends and risk factors for diabetes mellitus in cats presented to veterinary teaching hospitals. Journal of Felines Medicine and Surgery 2007;9(5):351–8.
- 179. Guptill L, Glickman L, Glickman N. Time tends and risk factors for diabetes mellitus in dogs: analysis of veterinary medical database records (1970–1999). Veterinary Journal 2003;165(3):240–7.
- 180. Fall T, Hamlin HH, Hedhammar A, Kämpe O, Egenvall A. Diabetes mellitus in a population of 180,000 insured dogs: Incidence, survival, and breed distribution. Journal of Veterinary Internal Medicine 2007;21:1209–16.

- Nelson RW. Diabetes mellitus. In: Ettinger SJ, Feldman EC, editors. Textbook of Veterinary Internal Medicine, 6th edn. Elsevier, St. Louis, MO; 2005. p. 1563–91.
- 182. Marmor M, Willeberg P, Glickman LT, Priester WA, Cypess RH, Hurvitz AI. Epizootiologic patterns of diabetes mellitus in dogs. American Journal of Veterinary Research 1982;43(3):465–70.
- Williams DA, Steiner JM. Canine exocrine pancreatic disease. In: Ettinger SJ, Feldman EC, editors. Textbook of Veterinary Internal Medicine, 6th edn. Elsevier, St. Louis, MO; 2005. p. 1482–8.
- 184. Watson PJ, Roulois AJ, Scase T, Johnston PE, Thompson H, Herrtage ME. Prevalence and breed distribution of chronic pancreatitis at post-mortem examination in first-opinion dogs. Journal of Small Animal Practice 2007;48(11):609–18.
- 185. Hänichen T, Minkus G. Retrospektive studie zur pathologie der erkrankungen des exokrinen pancreas bei hund und katze. Tierärztliche Umschau 1990;45:363–8.
- Newman S, Steiner J, Woosley K, Barton L, Ruaux C, Williams D. Localization of pancreatic inflammation and necrosis in dogs. Journal of Veterinary Internal Medicine 2004;18:488–93.
- Cook AK, Breitschwerdt EB, Levine JF, Bunch SE, Linn LO. Risk factors associated with acute pancreatitis in dogs: 101 cases (1985–1990). Journal of the American Veterinary Medical Association 1993;203(5):673–9.
- 188. Hess RS, Kass PH, Shofer FS, Van Winkle TJ, Washabau RJ. Evaluation of risk factors for fatal acute pancreatitis in dogs. Journal of the American Veterinary Medical Association 1999;214(1):46–51.
- Colliard L, Ancel J, Benet JJ, Paragon BM, Blanchard G. Risk factors for obesity in dogs in France. Journal of Nutrition 2006;136:1951S–4S.
- Edney AT, Smith PM. Study of obesity in dogs visiting veterinary practices in the United Kingdom. Veterinary Record 1986;118(14):391–6.
- 191. McGreevy PD, Thomson PC, Pride C, Fawcett A, Grassi T, Jones B. Prevalence of obesity in dogs examined by Australian veterinary practices and the risk factors involved. Veterinary Record 2005;156(22):695–702.
- 192. Kanchuk ML, Backus RC, Calvert CC, Morris JG, Rogers QR. Neutering induces changes in food intake, body weight, plasma insulin and leptin concentrations in normal and lipoprotein lipase-deficient male cats. Journal of Nutrition 2002;132:1730S–2S.
- 193. Colliard L, Paragon BM, Lemuet B, Bénet JJ, Blanchard G. Prevalence and risk factors of obesity in an urban population of healthy cats. Journal of Feline Medicine and Surgery 2009;11(2):135–40.
- Scarlett JM, Donoghue S, Saidla J, Wills J. Overweight cats: prevalence and risk factors. International Journal of Obesity and Related Metabolic Disorders 1994;18(Suppl. 1):22–8.
- 195. German A. The growing problem of obesity in dogs and cats. Journal of Nutrition 2006;13:19405S–65S.
- 196. Marshal W, Bockstahler B, Hulse D, Carmichael S. A review of osteoarthritis and obesity: current understanding of the relationship and benefit of obesity treatment and prevention in the dog. Veterinary Comparative Orthopaedics and Traumatology 2009;22(5):3339–45.

- 197. Hess RS, Kass PH, Shofer FS, Van Winkle TJ, Washabau RJ. Evaluation of risk factors for fatal acute pancreatitis in dogs. Journal of the American Veterinary Medical Association 1999;214(1):46–51.
- 198. Jeusette I, Daminet S, Nguyen P, Shibata H, Saito M, Honjoh T, et al. Effect of ovariohysterectomy and ad libitum feeding on body composition, thyroid status, ghrelin, and leptin plasma concentrations in female dogs. Journal of Animal Physiology and Animal Nutrition 2006;90(1–2):12–18.
- 199. Jeusette I, Detilleux J, Cuvelier C, Istasse L, Diez M. Ad libitum feeding following ovariohysterectomy in female Beagle dogs: effect on maintenance energy requirement and on blood metabolites. Journal of Animal Physiology and Animal Nutrition 2004;88(3–4):117–21.
- Houpt KA, Coren B, Hintz HF, Hilderbrant JE. Effect of sex and reproductive status on sucrose preference, food intake, and body weight of dogs. Journal of the American Veterinary Medical Association 1979;174(10);1083–5.
- Backus RC, Cave NJ, Keisler DH. Gonadectomy and high dietary fat but not carbohydrate induces gains in body weight and fat of domestic cats. British Journal of Nutrition 2007;98(3):641–50.
- 202. Nguyen PG, Dumon HJ, Siliart BS, Martin LJ, Sergheraert R, Biourge VC. Effects of dietary fat and energy on body weight and composition after gonadectomy in cats. American Journal of Veterinary Research 2004;65(12):1708–13.
- Fettman MJ, Stanton CA, Banks LL, Hamar DW, Johnson DE, Hegstad RL, *et al*. Effects of neutering on bodyweight, metabolic rate and glucose tolerance of domestic cats. Research in Veterinary Science 1997;62(2):131–6.
- 204. Kanchuk ML, Backus RC, Calvert CC, Morris JG, Rogers QR. Weight gain in gonadectomized normal and lipoprotein lipase-deficient male domestic cats results from increased food intake and not decreased energy expenditure. Journal of Nutrition 2003;133(6):1866–74.
- 205. Root MV, Johnson SD, Olson PN. Effect of prebueral and postpuberal gonadectomy on heat production measured by indirect calorimetry in male and female domestic cats. American Journal of Veterinary Research 1996;57:371–4.
- 206. Harper EJ, Stack DM, Watson TD, Moxham G. Effect of feeding regimes on body weight, composition and condition score in cats following ovariohysterectomy. Journal of Small Animal Practice 2001;42:433–8.
- 207. Flynn MF, Hardie EM, Armstrong PJ. Effect of ovariohysterectomy on maintenance energy requirements in cats. Journal of the American Veterinary Medical Association 1996;209:1572–81.
- 208. Hoenig M, Ferguson DC. Effects of neutering on hormonal concentrations and energy requirements in cats. American Journal of Veterinary Research 2002;63(5):634–9.
- Martin L, Siliart B, Dumon H, Backus R, Biourge V, Nguyen P. Leptin, body fat content and energy expenditure in intact and gonadectomized adult cats: a preliminary study. Journal Animal Physiology and Animal Nutrition 2001;85:195–9.
- Nijland ML, Stam F, Seidell JC. Overweight in dogs, but not in cats, is related to overweight in their owners. Public Health and Nutrition 2009;23:1–5.
- Olson PN, Kusstritz MV. Johnston SD. Early-age neutering of dogs and cats in the United States (a review). Journal of Reproduction and Fertility Supplement 2001;57:223–32.

- 212. Howe LM, Slater MR, Boothe HW, Hobson HP, Fossum TW, Spann AC, *et al.* Long-term outcome of gonadectomy performed at an early age or traditional age in cats. Journal of the American Veterinary Medical Association 2000;217(11):1661–5.
- 213. Howe LM, Slater MR, Boothe HW, Hobson HP, Holcom JL, Spann AC. Long-term outcome of gonadectomy performed at an early age or traditional age in dogs. Journal of the American Veterinary Medical Association 2001;218(2):217–21.