Evaluating the benefits and risks of neutering dogs and cats

Introduction

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 removal of the testes or ovaries, 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.[185,186]. 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 attitudes among pet owners and veterinarians towards neutering.[117,187-190]

While the primary purpose of surgical neutering is to prevent reproduction, like most medical interventions the procedure has other effects, both beneficial and undesirable. 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.[70,93,148-153]

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, and this is rarely available. However, consideration of the possible health consequences of these associations is warranted when offering owners recommendations concerning neutering.

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 etiologic significance of the risk factors identified.[191]

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.[192]

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.[193,194] In this review, I have attempted to provide estimates of 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 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.

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 the 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.

The role of the veterinarian in the decision whether or not to neuter a given pet is to provide the owner with accurate and relevant information based on the current best scientific evidence. This includes information about the degree of uncertainty inherent in the current evidence. Clients expect truthful, accurate scientific information from veterinarians, and they do not lose confidence when the truth entails uncertainty.[215-216] While the final decision rests with the owner, it is appropriate for veterinarians to utilize their knowledge and expertise to guide and inform this decision by relating the current best research evidence to the circumstances of the particular client and patient.

This review is an attempt to assist the veterinarian in this task by considering the totality of the scientific information currently available and drawing some pragmatic conclusions about the overall benefits and risks of neutering dogs and cats. This is a narrative review,

not a systematic review, so while it is thorough it may not be comprehensive or completely free of bias in the selection and evaluation of the studies discussed. Clinicians are encouraged to read the primary and review literature themselves and consider the unique circumstances of their practice and individual patients in making evidence-based recommendations.

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 United States has decreased from an estimated 23.4 million in 1970 to about 4.5 million by the year 2000 [1], 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.[2,55] Furthermore, intact cats and dogs are at increased risk of being given up by their owners, possibly because they exhibit unacceptable behaviors associated with being intact or because they result from unintended reproduction or are surplus offspring of other pets in the household. [3,4,202,209]. So neutering can both reduce the number of unwanted puppies and kittens and reduce 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 United States, most the product of unplanned

breeding.[1] There is a great deal of controversy over the welfare of feral cats and the impact they may have on wildlife and public health.[5-8] 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 unowned cats is a worthwhile goal.[5] Neutering of owned and feral cats, can promote this goal, though it is likely that neutering programs alone cannot fully control cat populations or reliably eliminate feral colonies.[7,57,201]

While populations of stray dogs have largely been eliminated in the United States and much of Europe, such populations still exist in many countries and represent a significant human health hazard.[1,196-197] There are many factors involved in controlling stray dog populations and the health risk they present.[196,200] Research suggests neutering alone is insufficient to control stray dog populations, but it is widely considered a vital component in such efforts. [195-199] It is important to inform owners that choosing not to neuter their pets involves accepting an additional responsibility to prevent unwanted reproduction and not exacerbate the problem of unowned dogs and cats being euthanized or living as strays with inadequate care.

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 fetuses and other material from infected females. The

incidence of this disease varies by country and region, from 1-18% in the United States to upwards of 25% in some countries. Clinical symptoms other than infertility are uncommon, though some dogs can experience serious infections of the bone, eyes, or nervous system. [9]

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.[10] One study in Sweden, using information from an insurance database of approximately 200,000 female dogs, most of which were intact, found that 2% of female dogs in the sample experienced a dystocia, and the overall incidence was 5.7 cases/1000 dog years at risk.[11] The study population consisted of dogs covered by health insurance, 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.[12]

Though dystocia can be treated medically, the majority of dogs and cats require surgical treatment.[10-13] Most females recovery fully from cesarean sections, though the risks of such surgery are likely greater than those of a planned spay surgery due to 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 cesarean 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 toxemia, transient diabetes mellitus, uterine torsion, uterine rupture, and pregnancy-associated pyelonephritis can all be prevented by neutering in both dogs and cats.[13]

Mammary Neoplasia

Mammary tumors are very common in intact female dogs. The chances of developing a mammary tumor increase with age and vary with breed.[13,17] 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 tumors of 53.3%, with significant variation in risk by breed and age.[14] A study in the United Kingdom, looking at a population of both intact and spayed dogs in a health insurance database, found mammary tumors to be the second most common type of tumor, with an age standardized incidence of 205 tumor per 100,000 dogs per year, however no breakdown of this figure according to neuter status was reported.[15] A Swedish study found an incidence in intact females of 1% at 6yrs of age, 6% at 8yrs, and 13% at 10 years when the study was terminated.[16] The incidence of mammary tumors 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. [17,20] Mammary neoplasia is extremely rare in male dogs. [17]

About half of canine mammary tumors are malignant, whereas 85-90% of feline mammary tumors are malignant.[17,18] Mammary cancer is usually treated surgically, often with adjunctive post-surgical chemotherapy, and it is often fatal despite treatment, with 59% of dogs with malignant tumors in one study eventually dying of causes related to their cancer. [21]

It has been traditionally claimed that spaying dramatically reduces the risk of mammary tumors in both dogs and cats. In dogs the risk has been reported as 0.5% for females spayed before the first estrus, 8% for those spayed before the second estrus, and 26% for those spayed after the second estrus.[19] More recent epidemiologic evidence has also found a lower incidence of mammary neoplasia in neutered females compared with intact females.[217] However, other studies have reported highly variable rates of mammary neoplasia among different breeds and among dogs neutered at different ages. One study found a mammary neoplasia prevalence of 3.5% in female golden retrievers under 9 years of age who were neutered between 2 and 8 years old, and no mammary tumors in intact females or dogs neutered before two years of age.[218] However, the same study found a similar prevalence of 2% in female Labrador retrievers neutered between 2 and 8 years of age and no mammary tumors in females neutered before 2 years old, but a prevalence of 1.4% in intact females, very similar to the rate in late-neutered females.

A systematic review of the literature on neutering and mammary tumors in dogs found that most studies had a high risk of bias.[219] Of the fours studies with only a moderate

risk of bias, two found neutering to be protective against mammary neoplasia, and two found no association.

While the existing evidence does suggest neutering reduces the risk of mammary tumors in dogs, the quality of this evidence is low, and there is great variation among studies and populations. Strong or specific claims about the preventative value of neutering with respect to mammary neoplasia are not justified.

Neutering female dogs at the time of surgical removal of mammary tumors or within 2 years before diagnosis is associated with longer survival and reduced risk of tumor recurrence.[21,220]

In cats, there is considerably less evidence bearing on this subject. One study has reported those spayed prior to 6 months of age had a 91% reduction in mammary cancer risk, and the risk was reduced 86% in those spayed before 1 year.[20]

Pyometra

Pyometra is a bacterial infection of the uterus that occurs as a consequence of changes in the uterine environment brought about by repeated estrus cycles.[13] Pyometra can be treated medically, with resolution of infection reported in 46% to 95% of cases, with minimal short-term complications, and with relatively high rates of recurrence (20-28%) and subsequent fertility problems.[22-23,203-207] It is more commonly treated, and recurrence prevented, by spaying the affected dog.[13,204]

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.[24] Pyometra has been reported in cats, but no published figures regarding the incidence are available.

Mortality from pyometra treated surgically is variable, from 4.2-17% in dogs and 8% in cats.[13,218,221] Mortality rates associated with medical treatment of pyometra were not identified. However, such treatment would not be appropriate for critically ill patients, 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.[13] Ovariectomy is as effective as ovariohysterectomy in preventing pyometra.[25]

One study has documented an increase in the incidence of pyometra concurrent with a decrease in the rate of neutering in the population.[221] Over a five-year period, the rate of elective neuters as a percentage of female dog outpatient visits in the study facility declined from 11.7% to 9.1%. Over the same period, the annual incidence of pyometra

surgeries as a percentage of female dog outpatient visits increased from 1.8% to 2.9%. While this cannot be interpreted as demonstrating a cause/effect relationship, it does suggest the possibility that if neutering declines as a result of changing recommendations and evidence concerning other conditions, a possible consequence may be an increase in the occurrence of pyometra.

Neoplasia of Reproductive Organs

Tumors of the ovaries are uncommon in dogs and cats with reported incidences of 6.25% in dogs and between 0.7%-3.6% in cats. There are several different types of ovarian tumors with variable degrees of malignancy. Little reliable information exists regarding the mortality associated with these tumors.[26]

Uterine tumors are very rare in dogs and cats, accounting for fewer than 2% of feline tumors and fewer than 0.5% of all canine tumors. Tumors of the uterus can generally be successfully removed by spaying the animal, though recurrence and spread to other organs has been reported.[26]

Tumors of the vulva or vagina in female dogs are not common, though they represent 2-3% of all canine tumors. 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 tumor removal. [26-28,144] Most vulvar and vaginal tumors are benign and can be cured by surgical removal, though the minority that are malignant have a poor prognosis and often recur or metastasize.[26]

Various rates of occurrence have been reported for testicular tumors, but random samples of testicles from dogs autopsied for reasons not related to testicular disease have shown that 16-27% of dogs had tumors, and many of these had more than one.[29] The testicles are the second most common site for cancer in intact male dogs.[145] Cryptorchid testicles are more likely to develop tumors, especially in dogs under 10 years of age.[30,31]

There are several types of testicular tumors. Most are slow to metastasize, with fewer than 15% of affected dogs showing spread to other organs. Some testicular tumors produce hormones, including estrogen which can cause feminization and bone marrow hypoplasia. Castration is the treatment of choice for testicular neoplasia, and it is usually curative. [13,26]

Prostate Disease

The most common disease of the canine prostate is benign prostatic hyperplasia (BPH).[13,32] This incidence of this disorder increases with age, from 15-40% for dogs under 7 years of age to 60-100% of dogs over 7 years of age.[32-34] While most dogs have few symptoms from BPH, some will experience difficulty urinating or defecating or bloody preputial secretions. BPH is a predisposing and complicating factor for prostatitis. [13] Prostatitis has been reported to occur in up to 28.5% of intact male dogs.[32,35] 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.[13,32]

Behavioral Benefits

Behavioral problems are an important reason for relinquishment of pet dogs and cats by owners. [1,5,44] The most common problem behaviors include aggression towards people or other animals, inappropriate elimination, and fearful behaviors.[45] To the extent that neutering increases or reduces the risks for these behaviors 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 behavior 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 behavior has consisted of owner surveys or analyses of biting or other problem behaviors 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 behaviors in dogs and cats which illustrate the potential behavioral benefits and risks associated with neutering.

Most studies have found intact male dogs to be disproportionately involved in aggressive behavior, particularly interdog aggression.[46-47,51] Others have reported marked reductions in aggression and other problem behaviors in male dogs as an effect of castration. In one study, roaming behavior decreased 90%, aggression between males decreased 62%, urine marking decreased 50%, and mounting decreased 80% following castration[48], and several other studies have found similar results.[49,50,54] Some studies have also reported intact dogs to be more likely to bite humans than neutered animals.[51] One study of dog-bite related fatalities found the vast majority of these incidents involved male dogs and intact dogs.[222]

Castration also dramatically reduces fighting, urine spraying, and roaming in male cats and aggression in free-roaming female cats.[52-54,223] One of the few experimental, prospective studies in this area compared various physical and behavioral 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.[102]

Longevity

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 varies across studies.[58-61,63,146,147,217,224] One large retrospective survey of many different breeds found neutered males lived 14% longer than intact males and neutered females lived 26% longer than intact females.[217]

Smaller studies of individual breeds have been inconsistent. One retrospective survey study of Rottweiler dogs found an association between the length of time females remained intact and their odds of achieving exceptional longevity (defined as a lifespan ≥ 13years).[62] However, a previous study of the same population reported intact females lived an average of 7.5 years, compared to 9.8 years for spayed females.[71] A similar survey of Viszlas found no difference in overall mortality between intact and neutered individuals of either sex.

The implications of these studies for other breeds or for any general relationship between lifespan and neuter status is not clear. There are also many potentially confounding factors which make general conclusions about the effect of neutering on longevity, and specific predictions about the impact on individuals, tenuous at best. Neutered and intact animals often differ in the type of husbandry and health care they receive, their exposure to potential environmental variables associated with disease, their genetic makeup, and many other factors which influence longevity. At present, the evidence suggests that neutered dogs generally live longer on average than intact dogs, and that the relative frequency of specific causes of death differ between these groups. However, the specific role, if any, of hormonal changes associated with neutering in generating these differences is unclear.

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 cases were intact males, and an association with prostatic disease and prostatic hormones is suspected, so neutering is likely protective for this disorder.[41,56] Perineal hernias can be repaired surgically, with a recurrence reported in from 20-40% of 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.[42,208]

Perianal fistulas is a immune-mediated disease seen most commonly in German Shepherds and Irish Setters and rarely in other breeds. It occurs predominantely 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 affected patients. [43] Perianal fistulas are chronic and often causes significant discomfort. A variety of medical and surgical treatments are used, with reports of long-term resolution of the condition in from 30%-78% of cases.[212-214]

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%-33% of cases.[64-67,225]. The majority of these complications are minor and require no treatment. [64,67] Complication rates vary considerably from practice to practice and are generally reported to be higher in studies of surgeries performed by students in training.[64,67] Reported death rates are less than 0.1%.[64]

Neoplasia

Prostatic Neoplasia-

Prostate cancer in dogs has previously been reported to have an incidence of less than 1%[13], 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%.[32,35] Most prostatic tumors are malignant, with metastases reported in 40-80% of cases at the time of diagnosis.[13,36]. Prostate cancer is an aggressive cancer with a poor long-term prognosis.[30]

There is some uncertainty about the role of castration in prostate cancer development. All of the studies have been retrospective epidemiologic surveys of relatively small numbers of dogs with prostatic carcinoma (n=7-76). Some have found fewer prostate cancers in castrated dogs than in intact dogs [36-38]. However, others have found either no effect of castration on the rate of prostate cancers [39] or an increased risk for castrated dogs.[35,40] Canine prostatic adenocarcinomas arise predominantly from androgen-independent ductal epithelial cells, so it appears that unlike in humans androgens are not

responsible for the initiation or progression of prostatic cancers. However, it is unclear whether castration is overall beneficial, neutral, or a risk factor for the development of prostate cancer.[30,40]

Osteosarcoma-

Osteosarcoma is a bone tumor usually seen in large breed dogs.[68,69] Overall incidence has been reported as 0.2%, but for at-risk breeds rates of 4.4%-6.2% are often reported.[70,72] A rate of 12.5% was reported in one study of Rottweilers, though the authors suggested this might have been an overestimate. [71] Osteosarcoma is an aggressive cancer with a poor long-term prognosis, and it is generally treated with surgery and chemotherapy.[69]

Neutered dogs have been reported to be at higher risk for osteosarcoma than intact dogs.[68,71]. In one study of Rottweilers, no difference was found in 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.[71] 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. Studies in other breeds have often not included enough cases to distinguish any difference in osteosarcoma prevalence between neutered and intact individuals.[218,226] However, one large multi-breed retrospective did identify more cases of osteosarcoma in neutered

than intact dogs.[217] Table 3 lists the findings of several reports that have evaluated the impact of neuter status on osteosarcoma risk.

Hemangiosarcoma-

Hemangiosarcoma is a malignant neoplasm of vascular endothelial cells.[73] The true incidence is unknown, but it makes up 5% of all non-skin cancers in dogs.[73] It is less common in the cat, found in 0.5% of cats autopsied and 2% of cancers in this species.[73] 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.[73,74,76] Primary cardiac hemangiosarcoma can also occur, with a reported incidence of 0.19%.[75] 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.[73]

In dogs, retrospective cohort studies of multiple breeds have reported spayed females to have 2 times the risk of splenic hemangiosarcoma and 5 times the risk of cardiac hemangiosarcoma compared to intact females.[74,75] Castrated males were found to have no increased risk of splenic hemangiosarcoma[74] and only a slightly higher risk than that of intact males for cardiac hemangiosarcoma.[75]

Breed specific studies have found inconsistent results [218,224,226]. One retrospective study in golden retrievers found no effect of neutering on HSA occurrence in males or females neutered before 12 months of age but a strong increase in risk for females

neutered after 12 months of age.[226] However, a similar study of golden retrievers and Labrador retrievers found no association between HSA occurrence and neuter status for either sex in either breed.[218] Another study in Viszlas, based on online owner reports, found females and males neutered after 12 months of age to be at greater risk than intact dogs and males neutered earlier.[224]

Table 4 lists the findings of several reports that have evaluated the impact of neuter status on hemangiosarcoma risk. In general, most studies support the hypothesis that neutering increases the risk of HSA in females, at least in at-risk breeds. However, it seems less likely to be a significant factor in males.

Transitional Cell Carcinoma (TCC)-

Transitional cell carcinoma is a cancer of the lower urinary tract, usually found in the bladder and uncommonly in the urethra of dogs.[77] It represents 1%-2% of canine cancers and is rare in the cat.[77,78] 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.[77] It is more common in females than males, prevalence varies by breed, and neutered animals have been reported to be at greater risk than intact animals.[78,79,217]

Lymphosarcoma-

Malignant lymphoma is one of the most common hematopoietic tumors in dogs and cats. However, precise incidence varies dramatically by breed, age, region, and many other

factors. In dogs, the annual incidence of lymphoma has been reported from 11-3000/100,000. [15,227-228] There is less information on the incidence in cats, though one author has reported an annual rate of 160/100,000.[229] In dogs, the disease most commonly presents in its multicentric form, whereas in cats alimentary lymphoma is most common.[227,230-232] Lymphoma has been classified into different types with varied biologic behavior, response to therapy, and prognosis, however these distinctions are generally not considered in epidemiologic studies evaluating the relationship between neutering and lymphoma occurrence.[233-235]

Multi-agent chemotherapy is the most common treatment for lymphoma. In dogs, this is often quite successful, with remission rates greater than 80% reported and survival of 1 year or more common.[236] Similar treatment is employed for cats with multicentric lymphoma, with outcomes that are similar, though not always as positive, as seen in dogs.[237-238] For the more common alimentary form, limited reports suggest variable and generally poor response to chemotherapy.[239]

Epidemiologic studies investigating associations between occurrence of lymphoma and neuter status have produced highly varied results (see Table 5). One case-control study in multiple breeds found a decreased risk for intact females, no clear difference in risk with neutering in females, and an increased risk in intact males with neutering being protective.[228] By contrast, another retrospective study in multiple breeds found an overall increase in lymphoma risk with neutering but did not evaluate sex differences.[217]

A number of recent studies in specific breeds have evaluated both sex differences and differences in risk of lymphoma with neutering at different ages. The results have also been quite variable. A study in Viszlas based on a web-based owner survey reported an increase in risk with neutering for both sexes and all ages at neuter.[224] One study in golden retrievers found an increase in lymphoma risk only for males neutered before twelve months.[226] A very similar study involving the same breed found an increase in risk for both males and females neutered between six and eleven months, but no difference in lymphoma occurrence for either sex neutered before six months or after one year.[218] This same study also evaluated the risk in Labrador retrievers and found no effect of neutering on lymphoma risk for either sex or any neutering age.

There is less information concerning the impact of neutering on the risk of lymphoma in cats. One retrospective study has found some evidence that intact individuals of both sexes may be at overall lower risk for intestinal tumors, of which lymphoma is the most common.[240] However, the authors caution that the this finding may be a result of confounding by age since neutered patients in that study were generally older than intact subjects.

The variability of these findings, even when the variety of types of lymphoma with different biologic behavior and response to therapy are not considered, emphasizes the tenuousness of any generalizations about the impact of neutering on the risk of this disease. Neutering does appear likely to have some impact on the risk of lymphoma. But

it will vary with sex, breed, age at neutering, and many other factors which have yet to be clearly elucidated. Further research is necessary before clear, reliable recommendations can be offered to dog and cat owners regarding the likely effect of neutering on the lymphoma risk for specific individuals.

Mast Cell Neoplasia-

Mast cell tumors (MCT) are among the most common skin tumors in dogs and cats. Incidence rates of 129-265/100,000 have been reported for dogs, though the occurrence of MCT varies dramatically by breed.[15,241-244] MCT are classified by a number of different schemes, and the prognosis is associated with classification status.[245-246] Surgical resection is the most common initial therapy, though chemotherapy and radiation are also employed in some circumstances.[247-248] Therapy is generally very successful, depending on histologic grade, completeness of surgical margins, and other factors, and MCT can often be cured.[244-248]

A number of studies have evaluated the relationship between occurrence of MCT and neuter status (see Table 6).[217-218,224,226,229] Most have found an increased risk of MCT in neutered females, with the exception of the results for Labrador retrievers. About half of the studies have found no difference in MCT occurrence between neutered and intact males, and the remainder have found higher risk in neutered males. A few studies stratifying for age at neutering appeared to find greater risk in the individuals neutered after one year of age compared with those neutered earlier.

Orthopedic Disease Risk

Cranial Cruciate Ligament Disease-

Rupture of the cranial cruciate ligament (CCL) 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%.[80-82,86] Cruciate ligament rupture is treated with a variety of surgical approaches, and it has an excellent long-term prognosis.[83,84]

In addition to breed and obesity, numerous studies report that neutering is associated with an increased risk of cranial cruciate ligament rupture, [80,81,82,86,218,226] However, there are studies that have not found such an association, overall or in some subpopulations. For example, one retrospective study of Golden retrievers and Labrador retrievers found an increased risk of CCL in all neutered males and females except those neutered between twelve and twenty-three months of age.[218] The same study found no increase in risk with neutering for Labradors except in males neutered before six months of age. (Interestingly, another study has suggested that the risk for CCL may be increased by early neutering due to changes in the conformation of the stifle joint.)[85] One case control study conducted in the United Kingdom found a crude association between neutering and CCL (OR=1.57, 95% CI=1.157-2.145, p=0.004), however this association was no longer significant once multivariable regression was conducted to control for confounding.[250] Overall, the preponderance of the evidence does suggest that neutering increases the risk of CCL, at least in some populations.

Hip Dysplasia-

Hip dysplasia (HD) is a developmental abnormality of the hip joint that can result in arthritis and clinical discomfort. It is rare in small breeds, with fewer than 1% of dogs affected, but it can be seen in as many as 40%-75% of large breed dogs.[86-89] Hip dysplasia is estimated to lead to clinically significant arthritis is fewer than 5% of 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.[89] The incidence of hip dysplasia is most strongly associated with breed and family history.[86,90,91].

Hip dysplasia can be treated if detected early with surgical therapies that reduce the chances of clinically significant arthritis later in life.[94,95] In older dogs who have already developed arthritis and clinical symptoms, these can be managed surgically or medically, with medications, weight reduction, and other therapies.[96-98] 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.[99,100]

Some studies have identified neutering as increasing the risk of hip dysplasia.[86,92,226]. The age at neutering may also be a factor influencing the development of hip dysplasia.[93,226] It is not completely clear if the increased risk is directly due to the effects of neutering or due to an increased incidence of obesity in neutered dogs, though the apparent increased risk associated with neutering persists when body condition score is controlled for in some studies.

There is some variation in the associations reported between neutering and HD in different populations. One study of golden retrievers found a significant increase in risk for males with neutering before twelve months of age, but no such increase in males neutered later or females neutered at any age.[226] A similar study of golden and Labrador retrievers found an increased risk in male golden retrievers neutered before one year and after two years but not in females or males neutered between 12 and twenty-three months.[218] In contrast, the same study found no association between neutering and HD in males but an increase in risk for females neutered at less than two years of age. Nevertheless, there is a trend towards greater occurrence of HD among neutered dogs compared to intact dogs in most studies investigating this relationship.

Femoral Capital Physeal Fracture-

A number of studies have found a large majority of spontaneous femoral capital physeal fractures in cats occur in obese neutered males.[179-182] It is clear that neutering delays closure of the growth plates in male cats[183], 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.

Behavioral Risks

Aggression-

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 behavior. A number of studies of dogs referred for treatment of behavior problems have identified a higher proportion of spayed than intact females among animals exhibiting aggression.[46,51] 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.[184] 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.

It has also been reported 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 behaviors were not observed in those females who were spayed and had not shown aggressive tendencies prior to the procedure.[103] 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.[101] How reliable such an owner survey might be or how applicable to other breeds is unclear.

Reactivity-

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

presence of unfamiliar humans and dogs than were intact dogs.[104]. 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 behavioral differences between the groups.[105] The clinical significance or applicability of these findings to behavior problems is unclear.

Dementia-

One study has examined the relationship between neutering and the development of age-related behavioral changes thought to be similar to Alzheimer's disease or other forms of senile dementia in humans.[106] Such changes are relatively common, being reported in 28% of dogs 10-12 years old and 68% of dogs 15-16 years old.[107] 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.[107] 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-

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.[93,108-111] Medical treatment is reported to successfully control the symptoms in 65-75% of dogs.[108,112,210-211] A systematic review of studies evaluating the effect of neutering on the risk of urinary incontinence concluded that while there is some evidence that neutering increases the risk of incontinence, and earlier neutering may be more likely to do so that later neutering, overall the evidence is weak and at significant risk of bias, so no firm conclusion can be reached.[251]

Urinary Tract Infections-

Two retrospective reports, one of dogs with persistent urinary tract infections and one very large study of nearly 11,000 dogs with uroliths removed submitted to a university laboratory for analysis, have found spayed females to be at increased risk for urinary tract infections compared to intact females.[113,114] However, one case-control study of 78 dogs with naturally acquired urinary tract infections did not find such a relationship.[115] No association with urinary tract infections has been found for neutering of male dogs.[113]

Feline Lower Urinary Tract Disease-

Feline Lower Urinary Tract Disease (FLUTD) is a collection of symptoms ranging from mild hematuria and stranguria to potentially life-threatening urinary tract obstruction.[116] Causes include idiopathic interstitial cystitis, urinary tract infection, urolithiasis and neoplasia.[116] FLUTD has been reported to occur in 1.3%-4.6% of cats in private practice and 7%-8% of cats in veterinary teaching hospitals.[117,118] While some studies have found no association between FLUTD conditions and neutering

[70,119], and it does not appear that neutering affects the size of the urethra in male cats (a possible risk factor for obstruction)[120], several epidemiologic studies have found that neutering status does raise the risk of some causes of FLUTD.[121,122]. Castrated males were at an increased risk compared to intact males for all causes of FLUTD except infection and urinary incontinence. Spayed females had an increased risk for urolithiasis, urinary tract infections, and urinary tract tumors, but not other causes of FLUTD. Intact females had a decreased risk for most causes.[122] 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% of cats with FLUTD symptoms, and the risk is higher in castrated males cats.[122,123]

Hypothyroidism-

Hypothyroidism is usually due to autoimmune thyroiditis or idiopathic thyroid atrophy.[124,125] It occurs in an estimated 0.2%-0.3% of dogs.[126,127] An epidemiologic survey of 3,206 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.[126,127] 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.[129] Supplementation of thyroid hormone resolves the disease symptoms in most cases.[127,128]

Diabetes Mellitus-

Diabetes mellitus is a multifactorial disease that has a variety of manifestations and sequelae. Incidence in cats has been reported from 0.08%-2%, with Burmese cats having a higher rate of occurrence than other breeds or mixed-breed cats.[131-134] Incidence in dogs is estimated at 0.19-0.64%, with significant breed variations.[135,136] 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.[132] However, when age and weight are controlled for no effect of neutering is seen in other studies.[134] In dogs, diabetes is often reported to be more common in females than males [130,136] though this is not found in all populations.[133]

Castrated males were at higher risk for diabetes than intact males in one study, though weight was not controlled for.[137] Some authors have suggested that intact females may be at greater risk of diabetes due to the antagonistic effects of ovarian hormones on insulin, and spaying is an important part of regulating diabetes in female dogs. [133] Obesity is clearly a risk factor for diabetes in cats, thought 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.[130-133,136] Diabetes is a serious chronic disease that can often be managed for long periods but cannot be cured.

Pancreatitis-

Pancreatitis can manifest as a chronic or acute disease with varying degrees of severity

and multifactorial causation.[138] The true incidence of pancreatitis is unknown, and although autopsy surveys have found evidence of inflammation in anywhere from fewer than 1% to more than 50% of dog pancreases, no study has reported the true incidence of clinical pancreatitis.[139-141] In dogs, there is some evidence that neutered animals may be at higher risk than intact animals for acute pancreatitis.[142,143]

Obesity-

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.[154-156] Among cats, an estimated 19%-40% are overweight and 7.8% are obese.[157-159] Being overweight is a significant risk factor for many serious diseases.[134,160-162]

Almost all studies agree that neutered cats and dogs are more likely to be overweight or obese than intact cats and dogs.[154-156,158-160,163-169,252-253] It is not clear, however, if the age at neutering has any impact on this risk. One study has reported a protective effect of early neutering, while others have found no association.[93,252,254]

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.[170-173] 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.[167-169,174] 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.[53,165,169,171,172]

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.[154,159,160,175]

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. [154,160]

Optimal Age for Neutering

For decades, the traditional age for neutering dogs and cats in the United States 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 anesthetic mortality in younger animals in the first half of the 20th century.[70] Anesthetic 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.[65,102,176]

In addition to the consideration of age at neutering in the studies referred to previously, several prospective studies have specifically investigated the potential effects of neutering at various ages. One large scale (775 cats and 1,213 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.[65] Another study followed 31 kittens neutered at 7 weeks and at 7 months for 1 year and found no differences in any measures of behavioral or physical development.[102] 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.[177,178] Of the numerous measures of health, behavior, 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.[177] 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.[178] Dogs in the traditional-neuter age group had more gastrointestinal problems than dogs in the early-neuter group.[178] 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.[111]

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 behavioral and medical outcomes.[93,149]

For dogs, 7 out of 14 behavioral measures appeared affected by age at neutering, with early-neutering worsening 3 problem behaviors and improving 4. Animals in the early-neuter group exhibited higher rates of noise phobia and sexual behaviors. The early-neutered group also exhibited less separation anxiety, fearful urination in the house, and escaping. Early-castrated males (but not females) showed more aggression towards humans in the household and more barking. When only problems considered by owners to be serious were analyzed, the reduced risk of escaping for the early-neuter group was the only behavior still significantly associated with age at neutering.[93]

Of the medical conditions monitored, 4 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-neuter group. Rates of cystitis and urinary incontinence were higher for females neutered before 5.5 months of age. The early-neuter group had lower rates of respiratory infections but higher rates of parvoviral infection. And finally, the early-neuter 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.[93]

In the feline study, early neutering increased shyness around strangers for both sexes, and it increased hiding behavior 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 behaviors. 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 artifact. When only problems considered serious were analyzed, none of these behaviors was significantly associated with age at neuter.[149]

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.[149]

Considering the very large number of medical and behavioral conditions examined in the four retrospective studies of shelter animals, 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 behavioral 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 due to 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.

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 etiologic factors involved in most serious behavioral 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 estrus and reproduction for both cats and dogs. It also appears to increase the risk of a number of medical and behavioral conditions. Many of these are relatively uncommon or easily treated, but some are serious and common in some breeds. In particular, there is limited but growing evidence that in breeds at significant risk for cancers such as osteosarcoma, hemangiosarcoma, lymphosarcoma, and mast cell neoplasia, neutered females are often reported to have an increased risk of these diseases.

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, but of course 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 clearly greater than the risks. In the absence of established problems with aggression, roaming, or prostate disease, it does not appear that neutering has predictable health benefits for individual dogs. And while the potential of increased cancer risk appears less significant for males than females, other breed-specific risks, such as that of cruciate ligament disease, are likely greater in neutered males. The population benefits, of course, argue in favor of routine neutering of male dogs. However, in terms of individual health, a strong case can be made for not routinely neutering male dogs.

For male cats, the evidence is limited in quantity, but it appears that neutering confers more benefit than harm. Table 2 summarizes the effects of castration on males of both species. 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, so no strong recommendation for or against the practice can be made.

Prospective studies tend to find few differences in health outcomes for cats and dogs neutered at different ages. Retrospective studies are mixed, with some identifying increases in specific health risks with earlier neutering ages and others reporting greater risk in dogs neutered later. The lack of clear and consistent associations between age at neutering and particular medical or behavioral outcomes despite several large studies suggests that broad generalizations about the health risks associated with neutering at particular ages are unjustified. However, there is some evidence that age at neutering may be a significant factor for particular health risks in particular populations. Sex, breed, and other factors may interact with age at neutering to influence health outcomes. In the future, as the evidence develops, the emphasis of veterinarians in making recommendations about neutering should be on developing individualized risk profiles rather than promoting simple, general guidelines for all patients.

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 light of the individual circumstances and characteristics of each animal.

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Table 1: Effects of Neutering 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, cat	significant pet overpopulation and associated euthanasia
Risks of reproduction	Uncommon	Variable	Prevents	dog, cat	dystocia, brucellosis, diabetes, others; risk of dystocia can be high for certain breeds
Mammary neoplasia	Very Common	Very	Probably ↓	dog, cat	generally poor prognosis
Pyometra	Very Common	Very	Prevents	dog, cat	
Uterine neoplasia	Rare	Variable	Prevents	dog, cat	some benign/removable, some malignant
Ovarian neoplasia	Uncommon	Variable	Prevents	dog, cat	
Vaginal/Vulvar neoplasia	Uncommon	Moderate	↓ dramatically	dog	
Osteosarcoma	Uncommon	Very	Possibly ↑	dog	risk variable by breed
Hemangiosarcoma	Uncommon	Very	Probably ↑	dog	risk variable by breed
Lymphosarcoma	Uncommon	Very	Possibly ↑	dog	risk variable by breed
Mast Cell Neoplasia	Common	Moderate	Probably ↑	dog	risk variable by breed, often curable
Transitional cell carcinoma	Uncommon	Very	↑	dog	risk variable by breed
Cruciate ligament disease	Common	Moderate	↑	dog	risk variable by breed, surgically treatable
Hip dysplasia	Common	Moderate	Probably ↑	dog	risk variable by breed
Aggressive behavior	Common	Very	Possibly ↑	dog, cat	
Urinary incontinence	Very Common	Mild	Possibly ↑	dog	medically controllable in 65-75% of cases
Urinary tract infection	Common	Mild	Possibly ↑	dog	easily treatable
Hypothyroidism	Uncommon	Moderate	Possibly ↑	dog	easily treatable
Diabetes mellitus	Uncommon	Very	Possibly ↑	dog, cat	risk variable by breed
Acute pancreatitis	Uncommon	Very	Possibly ↑	dog	
Obesity	Common	Very	↑	dog, cat	easily prevented by calorie restriction
Longevity	--	--	Possibly ↑	dog, cat	neutering influences causes of death

↓=decreases/reduces, ↑=increase/exacerbates

Table 2: Effects of Neutering 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, cat	significant pet overpopulation population and associated euthanasia
Testicular neoplasia	Uncommon	Moderate	Prevents	dog	most benign and surgically removable
Prostate disease	Very Common	Variable	↓ dramatically	dog	some have few symptoms others have severe, chronic disease
Behavior problems	Common	Variable	Variable	dog, cat	conflicting studies; most report less aggression, roaming, urine marking
Perineal hernias	Uncommon	Moderate	↓	dog	can often be repaired surgically
Perianal fistulas	Uncommon	Moderate	↓	dog	incidence varies by breed, some respond well to treatment others are serious chronic problem
Prostatic neoplasia	Uncommon	Very	Probably ↑	dog	poor prognosis
Osteosarcoma	Uncommon	Very	Possibly ↑	dog	risk variable by breed
Hemangiosarcoma	Uncommon	Very	Probably no effect	dog	risk variable by breed
Lymphosarcoma	Uncommon	Very	Unclear	dog	risk variable by breed
Mast Cell Neoplasia	Common	Moderate	Probably no effect	dog	risk variable by breed, often curable
Cruciate Ligament Disease	Common	Moderate	↑	dog	risk variable by breed, surgically treatable
Hip dysplasia	Common	Moderate	Probably ↑	dog	risk variable by breed, common in a few breeds
Femoral physeal fracture	Uncommon	Moderate	Possibly ↑	cat	obesity may be confounding factor
Hypothyroidism	Uncommon	Moderate	Possibly ↑	dog	easily treatable
Diabetes mellitus	Uncommon	Very	Possibly ↑	dog, cat	risk variable by breed
Acute pancreatitis	Uncommon	Very	Possibly ↑	dog	
Obesity	Common	Very	↑	dog, cat	easily prevented by calorie restriction
Longevity	--	--	Possibly ↑	dog, cat	neutering influences causes of death

↓=decreases/reduces, ↑=increase/exacerbates

Table 3: Cited reports examining the relationship between neuter status and risk of osteosarcoma in dogs

Study	**More Common Neutered**	**More Common Intact**	**No Difference**	**Comments**
Ru, G. 1998	Overall OR=2.2			Purebred dogs only, case-control study
Cooley, D. 2002	Males neutered <1yr RR=3.8 (95% CI=1.5-9.2) Females neutered <1yr RR=3.1 (95% CI=1.1-8.3)		Males neutered 1-3.5yrs RR=1.7 (95% CI=0.7–4.3) Males neutered >3.5yrs RR=1.4 (95% CI=0.6–3.5) Females neutered 1-5yrs RR=1.4 (95% CI=0.5–3.8) Females neutered >5yrs RR=1.2 (95% CI=0.4–3.2)	Rottweilers only, retrospective cohort
Hoffman, J.M. 2013	Overall			Multiple breeds/mixed-breeds, retrospective cohort

Table 4: Cited reports examining the relationship between neuter status and risk of hemangiosarcoma in dogs

Study	**More Common Neutered**	**More Common Intact**	**No Difference**	**Comments**
Prymak, C. 1988	Females OR=2.2 (95% CI=1.2-4.1)		Males	Splenic HSA only, retrospective cohort
Ware, W. 1999	Females RR=5.33 (95% CI=3.96-7.19) Males RR=1.55 (95% CI=1.21-1.98)			Differences not found for all breeds, retrospective cohort, cardiac HSA only
Torres de la Riva, G. 2013	Females neutered >12mos RR=6.1 (95% CI=1.18-31.37)		Males Females neutered <12mos	Golden retrievers only, retrospective cohort
Hart, B.L. 2014			All groups	Golden retrievers & Labrador retrievers, retrospective cohort
Zink, M.C. 2014	Males neutered >12mos OR=5.3 (95% CI=1.5-18.2) Females overall OR=9.0 (95% CI=2.8-29.4) Females neutered >12mos OR=11.5 (95% CI=3.5-38.5) Females neutered <6mos OR=6.0 (95% CI=1.7-21.3)		Males overall OR=0.6 (95% CI=0.3-1.4) Males neutered <6mos OR=2.0 (95% CI=0.6-7.3)	Viszlas only, online owner survey

Table 5: Cited reports examining the relationship between neuter status and risk of lymphosarcoma in dogs

Study	**More Common Neutered**	**More Common Intact**	**No Difference**	**Comments**
Villamil, JA. 2009	Intact Female OR=0.69 (95% CI=0.63-0.74)	Intact Male OR=1.32 (95% CI=1.24-1.41) Neutered Male OR=0.91 (95% CI=0.85-0.97)	Neutered Female OR=1.02 (95% CI=0.96-1.08)	Multiple breeds, matched case-control study, OR is for development of lymphoma in each sex category
Torres de la Riva, G. 2013	Males neutered <12mos		Females Males neutered >12mos	Golden retrievers only, retrospective cohort
Hoffman, J.M. 2013	Overall			Multiple breeds/mixed-breeds, retrospective cohort
Hart, B.L. 2014	Male & Female Goldens neutered 6-11mos		Males and Female Goldens neutered <6mos and >1year All Labradors	Golden retrievers & Labrador retrievers, retrospective cohort
Zink, M.C. 2014	Overall OR= 4.3 (95% CI=1.9-9.7) Neutered <6mos OR=3.5 (95% CI=1.3-9.6) Neutered 7-12mos OR=3.1 (95% CI=1.0-9.4) Neutered >12mos OR=5.2 (95% CI=2.2-12.0)			Viszlas only, online owner survey, OR reference category is intact animals

Table 6: Cited reports examining the relationship between neuter status and risk of mast cell neoplasia in dogs

Study	**More Common Neutered**	**More Common Intact**	**No Difference**	**Comments**
White, CR. 2011	Females OR=4.11 (95% CI=2.19–7.69)		Males OR=1.37 (95% CI=0.90–2.09)	Case/control study, multiple breeds
Hoffman, J.M. 2013	Overall			Multiple breeds/mixed-breeds, retrospective cohort
Torres de la Riva, G. 2013	Females 2.3% of neutered <12mos 5.7% of neutered >12mos No cases in intact		Males 1.7% of neutered <12mos 4.2% of neutered >12mos 2.8% of intact	Golden retrievers only, retrospective cohort
Hart, B.L. 2014	Female Goldens neutered <6mos & >1yr		All Golden Males All Labradors	Golden retrievers & Labrador retrievers, retrospective cohort
Zink, M.C. 2014	Overall OR=3.5 (95% CI=2.3-5.4) Neutered <6mos OR=2.8 (95% CI=1.6-5.0) Neutered 7-12mos OR=2.0 (95% CI=1.1-3.9) Neutered >12mos OR=4.5 (95% CI=2.9-7.0)			Viszlas only, online owner survey, OR reference category is intact animals