Reference Point

Determining the optimal age for gonadectomy of dogs and cats

Margaret V. Root Kustritz, DVM, PhD, DACT

Elective gonadectomy of dogs and cats, most commonly performed as an OHE of females and castration of males, is one of the most common veterinary procedures performed in the United States.[1] Increasingly, dog owners and members of the veterinary profession throughout the world have questioned the optimal age for performance of these surgeries or whether they should even be performed as elective surgeries. The objective for the information reported here was to provide a review of the scientific evidence, which could be used by veterinarians to counsel clients appropriately on this issue.

Traditional Age at Gonadectomy

Currently, most veterinarians in the United States recommend that elective gonadectomy be performed in dogs and cats at 6 to 9 months of age. However, there does not appear to be any scientific evidence to document that this is the optimal age. In fact, the age at which pets have traditionally been spayed and neutered has varied through the years and with geographic location. In the early 1900s, OHE was performed at 3 to 6 months of age and castration as early as 4 weeks of age.[2] Over time, the recommended age for elective gonadectomy of small animals increased to 6 to 9 months of age. It has been hypothesized that this was the result of an increasing popularity of dogs and cats as pets as American citizens found themselves with more disposable income, a subsequent desire by those pet owners for reproduction control in their animals, and the intent of veterinarians to provide the safest possible anesthesia and surgery for these new "family members." Despite great advances in anesthetic and surgical techniques and multiple studies that provide evidence for the safety of anesthesia and surgery in dogs and cats of younger ages, veterinarians in the United States still cling to the recommendation to perform gonadectomy at 6 to 9 months of age, with the added stipulation that bitches and queens should be spayed before their first estrus.

In some parts of the world, elective gonadectomy is considered unethical and is strongly discouraged or disallowed by professional veterinary associations.[2] Elective gonadectomy is illegal in at least 1 country.[3] In 1 article[4] published in Europe, elective gonadectomy is decried as "the tool of despots and tyrants throughout history," and the author of that article claims that gonadectomized dogs are "canine eunuchs, condemned to live their lives in a physical and mental twilight." That author also questions how a profession that publicly declares itself the guardian of animal welfare can, with impunity, perform elective surgery on animals for human convenience.[4]

Cultural and personal factors, including religious affiliation, ethnic background, intended working life of the animal, urban or rural location of the household, and literacy status, also may be associated with the likelihood that an owner will request gonadectomy for a pet.[5-7] Species and sex also play a role; in retrospective surveys, cats are more likely to be spayed or castrated than dogs, and bitches and queens are more likely to have undergone elective gonadectomy than stud dogs or tomcats.[6-9]

Surgical and anesthetic techniques for elective gonadectomy in dogs and cats of various ages are provided in the veterinary literature.[10-12] The reported incidence of postoperative complications in 1,016 dogs and 1,459 cats after elective surgery was 6.1% and 2.6%, respectively, with most of these considered minor problems, including inflammation at the incision site and gastrointestinal tract upset.[13] Complications were more common in dogs that underwent surgery when they were > 2 years of age.[13] In a study[14] in which investigators evaluated complications in 142 dogs undergoing OHE performed by fourth-year veterinary students, incidence of intraoperative complications was 6.3% and incidence of postoperative complications was 14.2%. Again, most of these were minor, including self-resolving hemorrhage and inflammation at the incision site and gastrointestinal tract upset. In that study,[14] the high incidence of postoperative complications was associated with an increase in surgery time, which was in turn positively correlated with increasing body weight of the animal. In studies[15-17] in which incidence of intraoperative and postoperative complications for elective gonadectomies performed at various ages was compared, the only com-

ABBREVIATIONS

OHE	Ovariohysterectomy
TCC	Transitional cell carcinoma
CCL	Cranial cruciate ligament
FLUTD	Feline lower urinary tract disease
BPH	Benign prostatic hypertrophy-hyperplasia

From the Department of Veterinary Clinical Sciences, College of Veterinary Medicine, University of Minnesota, Saint Paul, MN 55108.

plication associated with age at time of surgery was an increased incidence of postoperative infectious disease in dogs undergoing elective gonadectomy when they were < 12 weeks old. This may have been an artifact of the source from which dogs were recruited for the study.[17]

Societal Benefits of Elective Gonadectomy

The primary societal benefits of elective gonadectomy in dogs and cats are fewer animals relinquished to humane organizations and the fact that a specific animal's contribution to pet overpopulation is minimized. Multiple studies[9,18-20] have revealed that sexually intact dogs and cats are more likely to be relinquished to humane organizations than are those that are gonadectomized. In only 1 study[21] was it reported that there was an increased percentage of gonadectomized animals among those relinquished to humane organizations; animals in that study were relinquished for behavioral reasons, and it was considered likely that they had been gonadectomized as a possible treatment for behavioral problems, but with no subsequent improvement after surgery.

Millions of dogs and cats are euthanized at humane organizations annually in the United States, with estimates of 5.4 to 9.1 million dogs and 5.7 to 9.5 million cats euthanized in 1990.[22,23] Crude estimates of annual death rates in dogs and cats are 7.9% and 8.3%, respectively.[24] Statistics from humane organizations housing at least 100 animals/y, combined with these death rates, suggest that < 400,000 dogs and cats should be euthanized at humane organizations annually.[25] Not all animals euthanized at humane organizations are euthanized because of overpopulation[26]; however, the aforementioned study[25] indicates that > 2 million dogs and cats were euthanized at those shelters alone and substantiates the loss of animal life and stress to workers at humane organizations associated with overpopulation of dogs and cats in the United States.

Sexually intact animals adopted from humane organizations may be returned or may reproduce, both of which would repopulate those shelters. In 1 study,[8] 36.4% of relinquished animals were from unwanted litters. In a survey[24] of dog- and cat-owning households in the United States, 56% of 154 canine litters and 68% of 317 feline litters were unplanned. There is a lack of knowledge about reproduction among animal owners; the most common reason reported for the unplanned canine litters was that the owner did not know the bitch was in heat.[24] Up to 57% of bitch owners were unaware that bitches may cycle twice each year, up to 83% of cat owners were unaware that queens are seasonally polyestrous, and up to 61% of dog and cat owners were not certain or truly believed that their pet would be better if it had a litter before OHE was performed.[9,27,28]

Owners that adopt animals from humane organizations routinely sign a spay-neuter contract. However, compliance with such contracts is typically < 60%.[8,29] Up to 90% of veterinarians support mandatory gonadectomy of dogs and cats prior to adoption.[30] Few venues exist for educating veterinarians in early-age gonadectomy of dogs and cats, with most being self-taught.[30,31] Enhanced training of veterinarians in early-age gonadectomy and pediatric anesthetic techniques, mandatory gonadectomy of dogs and cats prior to adoption, and increased education of dog and cat owners about small animal reproductive physiology can only be of benefit in addressing these societal issues.

Benefits and Detriments of Elective Gonadectomy for Behavioral Concerns

Sexually dimorphic behaviors are those most commonly displayed by 1 sex, with mounting and urine spraying as primary examples.[32] Aggression may be a sexually dimorphic behavior. Most commonly, only those forms of aggression associated with the presence of females in estrus (aggression between females or between males housed with those females) are considered sexually dimorphic. Gonadectomy and the subsequent decrease in gonadal steroid hormones have been correlated with a decrease in sexually dimorphic behaviors.[18,33-37] Likelihood that gonadectomy will impact sexually dimorphic behaviors is not correlated with duration of the problem behavior and may or may not be associated with prior sexual experience of the affected animal.[35,36,38-41] Trainability of working dogs is not altered by gonadectomy and does not vary with age of the dog at the time of gonadectomy.[a]

Sexual behavior of male cats makes them extremely undesirable, and often unsafe, household pets.[42] A decrease in sexually dimorphic behaviors after castration of male cats is an extremely powerful benefit of elective gonadectomy. Sexual behaviors of queens, bitches, and stud dogs, although still possibly undesirable, are less commonly so severe as to make these animals untenable as household pets.

Nonsexually dimorphic behaviors are not typically affected by gonadectomy. One large-scale study[43] of dogs revealed a possible increase in noise phobias and decrease in separation anxiety and submissive urination associated with gonadectomy performed before the dogs were 5 months old.

An increase in reactivity toward humans with strange (unfamiliar) dogs and in aggression toward family members has been reported after OHE of bitches in several studies.[44-46] The reason for this possible tendency has not been defined but may be attributable to a decrease in estrogen and oxytocin concentrations, both of which may exert antianxiety effects in some species.[47] This tendency also may be a breed-specific phenomenon.

Cognitive function may be altered by gonadectomy. Comparison of the progression of cognitive dysfunction in sexually intact and castrated male dogs revealed a slowing of progression in sexually intact males.[48] Sample size was small in that study, with only 6 dogs in the sexually intact male group. Androgen deprivation has been associated with increased amyloid deposition in brains of humans and rodents and with decreased synapses in brains of rodents and nonhuman primates.[49] However, in a study[50] in which investigators directly examined brain tissue for DNA damage, a significantly greater percentage of neurons had extensive DNA damage in sexually intact Beagles than in castrated Beagles between 9 and 10.5 years of age.

Benefits and Detriments of Elective Gonadectomy for Various Conditions

Several conditions in dogs and cats can be impacted by elective gonadectomy, including neoplasia and orthopedic diseases. Knowledge of the benefits and detriments associated with elective gonadectomy enables veterinarians to provide the best counsel to clients and also to promote animal health.

Mammary gland neoplasms—Mammary gland neoplasms are the most common tumors of female dogs, with a reported incidence of 3.4%, and they are the third most common tumors of female cats, with a reported incidence of 2.5%.[51-55] Mammary gland neoplasms are the most common types of malignant tumors in dogs.[53] Mean percentage of mammary gland tumors in female dogs that are malignant is 50.9%.[53,56-58] In female cats, > 90% of mammary gland tumors are malignant.[53,59,60] Metastases are reported in up to 77% of dogs with mammary gland carcinomas, with the lungs being the site of metastasis in 30.8% of affected dogs.[61,62] In 1 study,[62] 59.7% of dogs in which a mammary gland tumor was diagnosed were euthanized at the time of diagnosis.

Increasing age and breed are risk factors for development of mammary gland neoplasms, with a mean age at diagnosis of approximately 10 years in dogs and cats.[52,63,64] Breeds reported to be at increased risk for developing mammary gland tumors include the Boxer, Brittany, Cocker Spaniel, Dachshund, English Setter, English Springer Spaniel, German Shepherd Dog, Maltese, Miniature Poodle, Pointer, Toy Poodle, and Yorkshire Terrier. Cat breeds reported to be at increased risk of tumor development are the Japanese domestic breeds and Siamese (**Table 1**).[52,64,65]

Maintenance of sexually intact status is a major risk factor for development of mammary gland tumors in dogs and cats.[60,66] Overall, sexually intact dogs and cats have 7 times the risk of developing mammary gland neoplasms when they get older, compared with the risk for spayed dogs and cats.[67] Compared with the incidence in sexually intact dogs, dogs spayed before their first estrus have a 0.5% risk, dogs spayed after 1 estrus have an 8.0% risk, and dogs spayed after 2 estrous cycles have a 26.0% risk of developing mammary gland neoplasms when they get older.[68] However, performing an OHE may even have a substantial sparing effect in older dogs, with a reduced but still evident reduction for mammary gland neoplasms in dogs spayed as late as 9 years of age.[69]

An exact cause-and-effect relationship between sexually intact status and mammary gland neoplasia has not been defined. Estrogen and progesterone have direct and indirect stimulatory effects on mammary gland tissue, and receptors for both hormones have been identified in normal and neoplastic mammary gland tissues.[69-71] In 1 report,[69] it was suggested that mammary gland neoplasms may be more likely to develop in bitches that had overt pseudopregnancy more than 3 times during their life, which would support the hypothesis that there is a hormonal effect or a direct effect of malignant transformation of metabolically active mammary gland tissue.

Prostatic neoplasms—The reported incidence of prostatic tumors in dogs is 0.2% to 0.6%, and prostatic neoplasms in dogs are almost always malignant adenocarcinomas.[72-74] There is neoplastic differentiation in tissues of ductal or urothelial origin, which are androgen-independent tissues.[75] However, castrated dogs are at an increased risk for development of prostatic neoplasms, with the increase in risk ranging from 2.4 to 4.3 times that of sexually intact male dogs (**Table 2**).[72,74-76] Mean age of dogs at diagnosis is approximately 10 years, with slightly younger dogs having prostatic adenocarcinoma with metastases to bones.[74,77,78] An exact cause-and-effect relationship has not been defined, but it has been suggested[75] that deprivation of androgens does not act to initiate neoplasia; rather, androgen deprivation permits progression of disease.

Other types of tumors—Testicular tumors are the second most common tumor type in dogs, with a reported incidence of 0.9%.[b] Mean age of dogs at diagnosis is approximately 10 years.[63,64,79] Most tumors are readily diagnosed during physical inspection. Malignancy is considered low for all types of testicular tumors; therefore, castration is curative.[80]

Ovarian and uterine tumors are uncommon in dogs and cats. Although malignant tumors of both tissues have been reported, metastasis is rare and OHE is curative in most situations.[81-84]

Table 1—Benefits and detriments of OHE for various conditions in female cats.

Condition	Incidence	Substantial morbidity?	Specific breeds at risk?
Benefits			
Mammary gland neoplasms	2.5% in all cats; greatly reduced when spayed before first estrus	Yes	Yes*
Ovarian or uterine tumors	Low	No	No
Pyometra	Increases with age	No	No
Detriments			
Complications of surgery	2.6%	No	No
Obesity	High	No	No
FLUTD	0.6%	No	No
Diabetes mellitus	0.5%	No	Yes†

*Japanese domestic breeds and Siamese. †Burmese.

Table 2—Benefits and detriments of gonadectomy for various conditions in male dogs.

Condition	Incidence	Substantial morbidity?	Specific breeds at risk?
Benefits			
Testicular neoplasms	0.9%	No	No
BPH or prostatitis	75%–80% by 6 years of age	No	No
Detriments			
Complications of surgery	6.1%	No	No
Prostatic neoplasms	0.2%–0.6%	Yes	No
TCC	< 1%	No	Yes*
Osteosarcoma	0.2%	Yes	Yes†
Hemangiosarcoma	0.2%	Yes	Yes‡
CCL rupture	1.8%	Yes	Yes§
Obesity	2.8%	No	Yes‖
Diabetes mellitus	0.5%	No	Yes¶

*Airedale Terrier, Beagle, Collie, Scottish Terrier, Shetland Sheepdog, West Highland White Terrier, and Wire Fox Terrier. †Doberman Pinscher, Great Dane, Irish Setter, Irish Wolfhound, Rottweiler, and Saint Bernard. ‡Boxer, English Setter, German Shepherd Dog, Golden Retriever, Great Dane, Labrador Retriever, Pointer, Poodle, and Siberian Husky. §Akita, American Staffordshire Terrier, Chesapeake Bay Retriever, German Shepherd Dog, Golden Retriever, Labrador Retriever, Mastiff, Neapolitan Mastiff, Newfoundland, Poodle, and Saint Bernard. ‖Beagle, Cairn Terrier, Cavalier King Charles Spaniel, Cocker Spaniel, Dachshund, Labrador Retriever. ¶Airedale Terrier, Cocker Spaniel, Dachshund, Doberman Pinscher, Golden Retriever, Irish Setter, Miniature Schnauzer, Pomeranian, and Shetland Sheepdog.

The most common tumor of the urinary tract of dogs is TCC of the bladder.[85-88] Overall incidence of TCC in dogs is reported to be, at most, 1% of all malignant tumors.[89] Breeds at increased risk for development of a TCC include the Airedale Terrier, Beagle, Collie, Scottish Terrier, Shetland Sheepdog, West Highland White Terrier, and Wire Fox Terrier (**Table 3**).[90] Gonadectomized animals have a risk for development of TCC approximately 2 to 4 times that of sexually intact animals.[85,86] An exact cause-and-effect relationship has not been defined.

Osteosarcoma is a highly malignant tumor, with a reported incidence of 0.2%.[64] Risk of development of osteosarcoma increases with age and may increase with increasing body weight.[91,92] Breeds reported to be at increased risk for development of an osteosarcoma include the Doberman Pinscher, Great Dane, Irish Setter, Irish Wolfhound, Rottweiler, and Saint Bernard.[91,93] In 1 study[92] in which historical data that consisted of owners' assessments of body condition score and body weight were used for analysis, incidence of osteosarcoma was not correlated with body weight. However, owner assessment of body condition score is poorly correlated with veterinarian assessment of body condition score.[94]

Gonadectomy can increase the risk of development of osteosarcoma by 1.3 to 2.0 times.[91,95] In 1 study[92] in which investigators evaluated 683 purebred Rottweilers, there was a significant increase in the incidence of osteosarcoma in female and male dogs that had undergone gonadectomy when < 1 year of age; however, the overall incidence of osteosarcoma in this population of dogs was much higher than that in the general population, which suggested a hereditary component. Furthermore, life span of dogs did not differ (mean ± SD life span of sexually intact and castrated male dogs was 9.3 ± 2.5 years and 9.2 ± 2.5 years, respectively) or was noticeably increased (mean life span in sexually intact and spayed female dogs was 7.5 ± 2.4 years and 9.8 ± 2.4 years, respectively) in gonadectomized dogs.[92] An exact cause-and-effect relationship has not been defined.

Hemangiosarcoma is the most common cardiac tumor in dogs, with a reported incidence of 0.2%.[96] Breeds at increased risk for development of hemangiosarcoma include the Boxer, English Setter, German Shepherd Dog, Golden Retriever, Great Dane, Labrador Retriever, Pointer, Poodle, and Siberian Husky, with large breeds (in general) at increased risk, compared with the risk for small breeds.[97] For both cardiac and splenic hemangiosarcoma, relative risk is increased for gonadectomized animals, with spayed females reportedly having 2.2 times the risk of splenic hemangiosarcoma and 5 times the risk of cardiac hemangiosarcoma, compared with the risk for sexually intact females, and castrated males having 2.4 times the risk, compared with the risk for sexually intact males.[96,98] An exact cause-and-effect relationship has not been defined.

Orthopedic abnormalities—Postmenopausal women or those who have undergone OHE have explicit concerns about osteoporosis. However, there is no decrease in mineral density of bone in dogs after OHE.[99-101]

Timing of closure of the physes of long bones is controlled in part by gonadal hormones. In both dogs and cats, gonadectomy at any age prior to physeal closure delays that closure and is associated with statistically significant, although not readily visible or clinically relevant, lengthening of associated long bones.[34,102-106] However, no specific correlation has been found between age at gonadectomy and incidence of long-bone fractures, including physeal fractures.[35] In 1 study,[107] there was an increase in the incidence of capital physeal fractures in the femurs of castrated male cats; however, the cats with fractures were also overweight.

Table 3—Benefits and detriments of OHE for various conditions in female dogs.

Condition	Incidence	Substantial morbidity?	Specific breeds at risk?
Benefits			
Mammary gland neoplasms	3.4% in all dogs; greatly reduced when spayed before first estrus	Yes	Yes*
Ovarian or uterine tumors	Low	No	No
Pyometra	15.2% by 4 years of age; 23% to 24% by 10 years of age	Yes	Yes†
Detriments			
Complications of surgery	6.1%	No	No
Aggression	Variable	Potentially	Yes‡
TCC	$< 1\%$	No	Yes§
Osteosarcoma	0.2%	Yes	Yes‖
Hemangiosarcoma	0.2%	Yes	Yes¶
CCL rupture	1.8%	Yes	Yes#
Obesity	2.8%	No	Yes**
Diabetes mellitus	0.5%	No	Yes††
Urinary incontinence	4.9%–20.0%; increased when spayed at < 3 months of age	No	Yes‡‡

*Boxer, Brittany, Cocker Spaniel, Dachshund, English Setter, English Springer Spaniel, German Shepherd Dog, Maltese, Miniature Poodle, Pointer, Toy Poodle, and Yorkshire Terrier. †Bernese Mountain Dog, Cavalier King Charles Spaniel, Chow Chow, Collie, English Cocker Spaniel, Golden Retriever, Rottweiler, and Saint Bernard. ‡English Springer Spaniel. §Airedale Terrier, Beagle, Collie, Scottish Terrier, Shetland Sheepdog, West Highland White Terrier, and Wire Fox Terrier. ‖Doberman Pinscher, Great Dane, Irish Setter, Irish Wolfhound, Rottweiler, and Saint Bernard. ¶Boxer, English Setter, German Shepherd Dog, Golden Retriever, Great Dane, Labrador Retriever, Pointer, Poodle, and Siberian Husky. #Akita, American Staffordshire Terrier, Chesapeake Bay Retriever, German Shepherd Dog, Golden Retriever, Labrador Retriever, Mastiff, Neapolitan Mastiff, Newfoundland, Poodle, and Saint Bernard. **Beagle, Cairn Terrier, Cavalier King Charles Spaniel, Cocker Spaniel, Dachshund, and Labrador Retriever. ††Airedale Terrier, Cocker Spaniel, Dachshund, Doberman Pinscher, Golden Retriever, Irish Setter, Miniature Schnauzer, Pomeranian, and Shetland Sheepdog. ‡‡Boxer, Doberman Pinscher, Giant Schnauzer, Irish Setter, Old English Sheepdog, Rottweiler, Springer Spaniel, and Weimeraner.

Hip dysplasia is a hereditary condition in dogs that affects females and males with equal frequency and can be controlled (to some extent) by environmental factors, including diet.[108-111] The reported incidence of hip dysplasia is 1.7%, with an increased incidence in large- and giant-breed dogs, most particularly in the Chesapeake Bay Retriever, English Setter, German Shepherd Dog, Golden Retriever, Labrador Retriever, Samoyed, and Saint Bernard breeds.[112] In 1 large study[43] of 1,842 dogs, there was an increased incidence of hip dysplasia in dogs spayed or castrated prior to 5 months of age; however, it was not clear whether the diagnosis of hip dysplasia was confirmed by a veterinarian in all affected dogs.

Rupture of the CCL is more common in women than in men and may be more likely to occur during certain phases of the menstrual cycle, which suggests a hormonal effect on joint stability.[113] Dog breeds reported to be at increased risk of CCL rupture include the Akita, American Staffordshire Terrier, Chesapeake Bay Retriever, German Shepherd Dog, Golden Retriever, Labrador Retriever, Mastiff, Neapolitan Mastiff, Newfoundland, Poodle, Rottweiler, and Saint Bernard.[114,115] Reported incidence of CCL rupture is 1.8%, and it reportedly is more prevalent in gonadectomized female and male dogs than in sexually intact dogs.[115-117] An exact cause-and-effect relationship has not been defined, but heredity plays a role in the predisposition toward CCL injury, as might body weight and body condition score. To my knowledge, there have been no studies for which the results would implicate alterations in physeal closure with subsequent asynchrony of long-bone growth and abnormalities in joint formation as a cause of CCL rupture in dogs.[115,118]

Obesity—Obesity is the most common nutritional disorder of dogs and cats, with a reported incidence of 2.8% among the entire dog population.[119] It is a multifactorial problem. Risk factors include breed, with an increased incidence of obesity in Beagles, Cairn Terriers, Cavalier King Charles Spaniels, Cocker Spaniels, Dachshunds, and Labrador Retrievers; housing; increasing age[6]; ownership by an overweight person or a person ≥ 40 years old; and, possibly, sex of the dog.[94,119-122]

The most commonly reported risk factor for obesity is gonadectomy, with spayed or castrated dogs and cats much more commonly designated by veterinarians as being overweight or obese, compared with the weight designations for sexually intact animals.[33,121-127] In 1 study,[128] 34% of castrated male and 38% of spayed female dogs were considered overweight or obese. It is unclear whether age at the time of gonadectomy has an effect on subsequent obesity. Studies[34,102,103] in dogs failed to detect differences in food intake, body weight, or depth of back fat when comparing dogs gonadectomized at 7 or 8 weeks of age and dogs gonadectomized at 7 months of age. A retrospective study[43] of 1,842 dogs revealed a decrease in the incidence of obesity in dogs gonadectomized prior to 5 months of age when compared with those gonadectomized at > 5 months of age. Similarly, although cats are more likely than dogs to become obese after gonadectomy, no correlation has been found between age at gonadectomy and final body weight or amount of body fat.[34]

Metabolic rate decreases after gonadectomy in cats.[125,126] A cause-and-effect relationship between gonadectomy and obesity in dogs is less clearly defined. Spayed female dogs have an increase in food intake and increase in indiscriminate appetite after OHE, compared with those of sham-operated or age-matched control dogs.[44,129] Estrogen may act as a satiety factor, which would explain these changes.[122] This does not address the correlation between obesity and castration in male dogs. In both dogs and cats, obesity is not a mandatory consequence of gonadectomy; instead, it is controllable with an appropriate diet, feeding regimen, and exercise regimen.[130]

Urinary tract disorders—Spayed female dogs reportedly have an increased risk of developing urinary tract infections.[43,131] A cause-and-effect relationship has not been defined.

Female dogs spayed before onset of puberty may be more likely to maintain a juvenile or recessed vulva. In 1 study,[104] bitches spayed at 7 weeks of age had a vulva with a more immature appearance, compared with the vulva in bitches spayed at 7 months of age. It is the author's experience that bitches spayed as adults will have vulvar atrophy, which achieves the same result. A juvenile vulva in an otherwise healthy dog is of no clinical relevance. Overweight bitches with a recessed vulva, especially those with concurrent urinary incontinence, are more likely to develop perivulvar dermatitis.

Male dogs castrated at 7 weeks of age had less penile development than did dogs castrated when they were older.[102] Male cats castrated before onset of puberty may have a decreased ability to extrude the penis.[132,133] Clinical relevance of this phenomenon is not known.

Feline lower urinary tract disease is a syndrome consisting of hematuria, dysuria or pollakiuria, and possible urethral obstruction and is most commonly classified as idiopathic. The reported incidence of FLUTD is 0.6%.[134] Despite numerous vehemently declared anecdotes of an increase in the incidence of urethral obstruction in male cats castrated when young, numerous studies[35,132,135] have failed to detect a correlation between gonadectomy of cats at any age and a decrease in diameter of the urethra or an increase in incidence of FLUTD, with or without urethral obstruction. In 1 large study,[136] investigators identified gonadectomy as a risk factor for development of FLUTD in both female and male cats and also identified an increased risk of development of FLUTD in overweight or obese cats. In that study, sexually intact female cats had a relatively reduced risk for development of FLUTD.

Urethral sphincter mechanism incompetence, formerly known as estrogen-responsive urinary incontinence, is a common problem of spayed female dogs.[137-139] The condition is evident with equal frequency in ovariohysterectomized or ovariectomized female dogs, with the reported incidence ranging from 4.9% to 20.0%.[43,138-140] Studies[17,141] have failed to detect a correlation between age at time of OHE and likelihood of developing incontinence. In a study[43] of 983 female dogs, bitches were significantly less likely to develop incontinence when spayed at > 3 months of age. Other risk factors include body weight, with dogs weighing ≥ 20 kg (44 lb) at increased risk; breed, with Boxers, Doberman Pinschers, Giant Schnauzers, Irish Setters, Old English Sheepdogs, Rottweilers, Springer Spaniels, and Weimeraners at increased risk and Labrador Retrievers at decreased risk in European studies; and urethral length or resting position of the urinary bladder.[137,140,142-145] An exact cause-and-effect relationship has not been defined, with research currently focusing on altered gonadotropin secretion after gonadectomy.[146-150] Typically, urethral sphincter mechanism incompetence is easily controlled with medical treatments.

Adrenal gland disease—To the author's knowledge, there are no reports of an increase in the incidence of adrenal gland disease associated with sexually intact status in dogs and cats. In the United States, almost all ferrets are gonadectomized when extremely young; the incidence of adrenal gland disease in ferrets is higher in the United States than in European countries where ferrets are not routinely spayed or castrated.[151,152] In 1 study[152] in Europe, a correlation was detected between age at gonadectomy and age at onset of adrenal gland disease, with ferrets gonadectomized at a younger age having clinical signs of adrenal gland disease earlier in life. Sexually intact ferrets also have adrenal gland disease.[153] Possible causes for this include lack of down-regulation of sex steroids or an increase in circulating concentrations of gonadotropins that causes adrenal gland hyperplasia and possibly contributes to neoplastic transformation.[154-156]

Pyometra—Incidence of pyometra in dogs and cats in the United States has not been reported, perhaps because of the prevalence of OHE in these species before they reach an age when they would be likely to develop pyometra. In other countries, 15.2% and 23% to 24% of bitches developed pyometra by 4 and 10 years of age, respectively.[157,158] Pyometra is more common in nulliparous bitches than in bitches with a history of carrying a pregnancy successfully to term.[158,159] There is a significant likelihood that cats will have clinical evidence of uterine disease when queens reach 5 years of age.[160] Dog breeds reported to be at increased risk of developing pyometra include the Bernese Mountain Dog, Cavalier King Charles Spaniel, Chow Chow, Collie, English Cocker Spaniel, Golden Retriever, Rottweiler, and Saint Bernard.[158,159] In animals with pyometra, OHE is curative, with reported mortality rates of 0% to 17% in dogs and 8% in cats.[161,162]

Nonneoplastic prostatic disease—Benign prostatic hypertrophy-hyperplasia is a common disorder in sexually intact male dogs. In 1 study,[163] investigators evaluated male dogs. Of 300 sexually intact male dogs, 231 (63.4%) had BPH; all castrated male dogs in that study had profound prostatic atrophy. Development of BPH is positively correlated with age.[164-166] By 2.4 years of age, half of all sexually intact dogs will have histologic or clinical evidence of BPH, with the incidence increasing to 75% to 80% by 6 years of age and 95% to 100% by 9 years of age.[164,166,167] In addition, BPH predisposes dogs to prostatitis.[168] Neither BPH nor prostatitis is commonly associated with substantial morbidity, and castration is an integral part of the treatment of both conditions.[169,170]

Endocrine disorders—The reported incidence of diabetes mellitus in dogs is 0.5%.[171] Risk factors include breed, with Miniature Poodles, Miniature Schnauzers, Pugs, Samoyeds, and Toy Poodles at increased risk; sex, with female dogs more commonly affected than male dogs; and increasing age.[171,172] In 1 study,[172] a possible increase in the risk of developing diabetes mellitus was detected in castrated male dogs; however, it was not defined whether this could have been associated with obesity in these animals. In cats, the reported incidence of diabetes mellitus is 0.4% and risk factors include breed, with Burmese cats at increased risk; sex, with males at increased risk; and increasing age.[173-175] Gonadectomized male and female cats have an increased risk, with gonadectomized cats having 8.7 times greater odds of developing diabetes mellitus than for sexually intact cats.[173,174]

The incidence of hypothyroidism in dogs is 0.2% to 0.3%.[176,177] A breed predisposition has been described for the Airedale Terrier, Cocker Spaniel, Dachshund, Doberman Pinscher, Golden Retriever, Irish Setter, Miniature Schnauzer, Pomeranian, and Shetland Sheepdog breeds.[176,177] Those studies[176,177] have revealed an increased risk of development of hypothyroidism for spayed female and castrated male dogs, compared with the risk for sexually intact dogs. A cause-and-effect relationship has not been defined. Hypothyroidism typically is easily controlled with medical treatment.

Life span—Life expectancy at birth for women in the United States is 80.4 years, whereas that for men is 75.2 years.[178] Results for dogs vary,[179-181] with females living longer than males in some studies and the reverse being found in other studies. Negative correlations have been detected between body weight and longevity and between height and longevity in dogs.[182] Several studies[179-181] have revealed an increase in longevity for gonadectomized animals when compared with that for sexually intact animals. In sockeye salmon, life span is significantly longer in fish castrated before gonadal development.[183] Results of these studies argue against the evolutionary theory, which holds that it is not prudent for a population to carry individuals that have aged past reproductive usefulness.[50] In dogs and cats, this may be a reflection of enhanced care of animals by owners who have made the investment of surgery or a decrease in risk-associated behaviors (such as roaming) in gonadectomized animals.

Conclusions

How does a veterinarian reconcile all of these data to make the best possible recommendation regarding optimal age at which to neuter male and female dogs and cats? The author provides the following assertions:

- Animals housed at humane societies should be treated as a population. Societal benefit resulting from gonadectomy of unowned dogs and cats in the United States outweighs all other concerns. Male and female dogs and cats should be spayed or castrated before being offered for adoption by humane organizations.
- Pets should be considered individually, with the understanding that for these pets, population control is a less important concern than is health of each animal. Dogs and cats should be maintained as household pets. Responsible owners should ensure that their pets are provided appropriate and regularly scheduled veterinary care.
- The behavior of most sexually intact male cats makes them undesirable or dangerous as pets. Because castration substantially reduces these sexually dimorphic behaviors, it is recommended that all male cats not intended for breeding be castrated prior to puberty and that all breeding males be castrated as soon as their use as a breeding male has ceased.
- For female cats and male and female dogs, veterinarians and owners must consider the benefits and detriments of gonadectomy for each animal (Tables 1–3). Factors to be considered include incidence of various conditions associated with gonadectomy; degree of morbidity, with substantial morbidity defined as a condition prevalent in > 1% of the population, associated with > 50% of the malignancy or mortality rates, or not easily controlled by noninvasive treatments or good husbandry; breed; and intended working or breeding life of each animal.

As an example, consider a discussion between a veterinarian and the owner of an 8-week-old female Labrador Retriever that is not intended for breeding. This dog would benefit greatly from OHE before her first estrus as a means of preventing mammary gland tumors, which are extremely common and cause substantial morbidity (Table 3). Because of her breed, detriments of OHE include an increased predisposition to CCL injury, hemangiosarcoma, and obesity. However, there is a low incidence of hemangiosarcoma, and obesity can be readily controlled with good husbandry, which leaves CCL injury as the most important possible detriment. Because the incidence of CCL rupture is lower than that of mammary gland neoplasia, a veterinarian may choose to recommend OHE and educate the owner about maintenance of optimal body condition and other management techniques that will minimize potential for CCL injury. An OHE should be performed before the dog's first estrus. To minimize the potential for development of urinary incontinence, the veterinarian may choose to wait to perform the OHE until after the dog has reached 3 months of age.

The information provided here on the risks and detriments of gonadectomy is not intended to promote or to minimize the importance of gonadectomy as a means of controlling animal populations or possible impacts on animal health or behavior of a specific animal. The veterinary profession recognizes the need for individual assessment of risk and benefit when evaluating vaccination protocols for animals. Elucidation of the genome in various species may lead to individualized diagnostic and treatment plans for each animal in the future. It behooves us as veterinarians dedicated to the provision of the best possible care for animals to educate clients and evaluate each animal carefully when making recommendations regarding gonadectomy.

a. Daniels R, Canine Companions for Independence, Delaware, Ohio: Personal communication, 2002.
b. Hahn KA, Vonderhaar MA, Teclaw RF. An epidemiological evaluation of 1202 dogs with testicular neoplasia (abstr). *J Vet Intern Med* 1992;6:121.

References

1. Greenfield CL, Johnson AL, Schaeffer DJ. Frequency of use of various procedures, skills, and areas of knowledge among veterinarians in private small animal exclusive or predominant practice and proficiency expected of new veterinary school graduates. *J Am Vet Med Assoc* 2004;224:1780–1787.
2. Salmeri KR, Olson PN, Bloomberg MS. Elective gonadectomy in dogs: a review. *J Am Vet Med Assoc* 1991;198:1183–1192.
3. Gunzel-Apel AR. Early castration of dogs and cats from the point of view of animal welfare. *Dtsch Tierarztl Wochenschr* 1998;105:95–98.
4. Coffey DJ. Sexual mutilation. *Vet Times* 1998;Dec:34.
5. Eze CA, Eze MC. Castration, other management practices and socio-economic implications for dog keepers in Nsukka area, Enugu State, Nigeria. *Prev Vet Med* 2002;55:273–280.
6. Manning AM, Rowan AN. Companion animal demographics and sterilization status: results from a survey in four Massachusetts towns. *Anthrozoos* 1992;5:192–201.
7. Mahlow JC. Estimation of the proportions of dogs and cats that are surgically sterilized. *J Am Vet Med Assoc* 1999;215:640–643.
8. Alexander SA, Shane SM. Characteristics of animals adopted from an animal control center whose owners complied with a spaying/neutering program. *J Am Vet Med Assoc* 1994;205:472–476.
9. New JG, Salman MD, Scarlett JM, et al. Shelter relinquishment: characteristics of shelter-relinquished animals and their owners compared with animals and their owners in US pet-owning households. *J Appl Anim Welf Sci* 2000;3:179–201.
10. Howe LM. Surgical methods of contraception and sterilization. *Theriogenology* 2006;66:500–509.
11. Howe LM. Prepubertal gonadectomy in dogs and cats—part I. *Compend Contin Educ Pract Vet* 1999;21:103–111.
12. Howe LM. Prepubertal gonadectomy in dogs and cats—part II. *Compend Contin Educ Pract Vet* 1999;21:197–201.
13. Pollari FL, Bonnett BN, Bamsey SC, et al. Postoperative complications of elective surgeries in dogs and cats determined by examining electronic and paper medical records. *J Am Vet Med Assoc* 1996;208:1882–1886.
14. Burrow R, Batchelor D, Cripps P. Complications observed during and after ovariohysterectomy of 142 bitches at a veterinary teaching hospital. *Vet Rec* 2005;157:829–833.
15. Howe LM. Short-term results and complications of prepubertal gonadectomy in cats and dogs. *J Am Vet Med Assoc* 1997;211:57–62.
16. Howe LM, Slater MR, Boothe HW, et al. Long-term outcome of gonadectomy performed at an early age or traditional age in cats. *J Am Vet Med Assoc* 2000;217:1661–1665.
17. Howe LM, Slater MR, Boothe HW, et al. Long-term outcome of gonadectomy performed at an early age or traditional age in dogs. *J Am Vet Med Assoc* 2001;218:217–221.
18. Patronek GJ, Glickman LT, Beck AM, et al. Risk factors for relinquishment of dogs to an animal shelter. *J Am Vet Med Assoc* 1996;209:572–581.
19. Mondelli F, Previde EP, Verga M, et al. The bond that never developed: adoption and relinquishment of dogs in a rescue shelter. *J Appl Anim Welf Sci* 2004;7:253–266.
20. Patronek GJ, Glickman LT, Beck AM, et al. Risk factors for relinquishment of cats to an animal shelter. *J Am Vet Med Assoc* 1996;209:582–588.
21. Salman MD, Hutchison J, Ruch-Gallie R, et al. Behavioral reasons for relinquishment of dogs and cats to 12 shelters. *J Appl Anim Welf Sci* 2000;3:93–106.
22. Nassar R, Talboy J, Moulton C. *Animal shelter reporting study 1990*. Englewood, Colo: American Humane Assoc, 1992;5.
23. National Council on Pet Population Study and Policy. *National shelter census: 1994 results*. Fort Collins, Colo: National Council on Pet Population Study and Policy, 1994;1–2.
24. New JC, Kelch WJ, Hutchison JM, et al. Birth and death rate estimates of cats and dogs in US households and related factors. *J Appl Anim Welf Sci* 2004;7:229–241.
25. National Council on Pet Population Study and Policy. *Shelter statistic survey, 1994–1997*. Available at: www.petpopulation.org. Accessed Jun 2, 2007.
26. Kass PH, New JC, Scarlett JM, et al. Understanding animal companion surplus in the United States: relinquishment of nonadoptables to animal shelters for euthanasia. *J Appl Anim Welf Sci* 2001;4:237–248.
27. Scarlett JM, Salman MD, New JG, et al. The role of veterinary practitioners in reducing dog and cat relinquishments and euthanasias. *J Am Vet Med Assoc* 2002;220:306–311.
28. Scarlett JM, Salman MD, New JC, et al. Reasons for relinquishment of companion animals in US animal shelters: selected health and personal issues. *J Appl Anim Welf Sci* 1999;2:41–57.
29. Eno M, Fekety S. Early age spay/neuter: a growing consensus. *Shelter Sense* 1993;Nov:1–7.
30. Spain CV, Scarlett JM, Cully SM. When to neuter dogs and cats: a survey of New York state veterinarians' practices and beliefs. *J Am Anim Hosp Assoc* 2002;38:482–488.
31. Root Kustritz MV, Johnston SD, Lieberman LL. Availability of training for prepuberal gonadectomy at North American veterinary colleges. *J Am Vet Med Assoc* 2000;216:1566–1567.
32. Hart BL, Eckstein RA. The role of gonadal hormones in the occurrence of objectionable behaviours in dogs and cats. *Appl Anim Behav Sci* 1997;52:331–344.
33. Stubbs WP, Bloomberg MS, Scruggs SL, et al. Effects of prepubertal gonadectomy on physical and behavioral development in cats. *J Am Vet Med Assoc* 1996;209:1864–1871.
34. Spain CV, Scarlett JM, Houpt KA. Long-term risks and benefits of early-age gonadectomy in cats. *J Am Vet Med Assoc* 2004;224:372–379.
35. Hopkins SG, Schubert TA, Hart BL. Castration of adult male dogs: effects on roaming, aggression, urine marking, and mounting. *J Am Vet Med Assoc* 1976;168:1108–1110.
36. Nielsen JC, Eckstein RA, Hart BL. Effects of castration on problem behaviors in male dogs with reference to age and duration of behavior. *J Am Vet Med Assoc* 1997;211:180–182.
37. Hart BL, Barrett RE. Effects of castration on fighting, roaming, and urine spraying in adult male cats. *J Am Vet Med Assoc* 1973;163:290–292.
38. Hart BL, Cooper L. Factors relating to urine spraying and fighting in prepubertally gonadectomized cats. *J Am Vet Med Assoc* 1984;184:1255–1258.
39. Rosenblatt JS, Aronson LR. The decline of sexual behavior in male cats after castration with special reference to the role of prior sexual experience. *Behavior* 1958;12:285–338.
40. LeBoeuf BJ. Copulatory and aggressive behavior in the prepuberally castrated dog. *Horm Behav* 1970;1:127–136.
41. Sakata JT, Jupta A, Gonzalez-Lima F, et al. Heterosexual housing increases the retention of courtship behavior following castration and elevates metabolic capacity in limbic brain nuclei in male whiptail lizards, *Cnemidophorus inornatus*. *Horm Behav* 2002;42:263–273.
42. Root Kustritz MV. Elective gonadectomy in the cat. *Feline Pract* 1996;24(6):36–39.
43. Spain CV, Scarlett JM, Houpt KA. Long-term risks and benefits of early-age gonadectomy in dogs. *J Am Vet Med Assoc* 2004;224:380–387.
44. O'Farrell V, Peachey E. Behavioural effects of ovariohysterectomy on bitches. *J Small Anim Pract* 1990;31:595–598.
45. Kim HH, Yeon SC, Houpt KA, et al. Effects of ovariohysterectomy on reactivity in German Shepherd Dogs. *Vet J* 2006;172:154–159.
46. Reisner IR. Dominance-related aggression of English Springer Spaniels: a review of 53 cases. *Appl Anim Behav Sci* 1993;37:83–84.
47. McCarthy MM, McDonald EH, Brooks PJ, et al. An anxiolytic action of oxytocin is enhanced by estrogen in the mouse. *Physiol Behav* 1997;60:1209–1215.
48. Hart BL. Effect of gonadectomy on subsequent development of age-related cognitive impairment in dogs. *J Am Vet Med Assoc* 2001;219:51–56.

49. Janowsky JS. The role of androgens in cognition and brain aging in men. *Neuroscience* 2006;138:1015–1020.
50. Waters DJ, Shen S, Glickman LT. Life expectancy, antagonistic pleiotropy, and the testis of dogs and men. *Prostate* 2000;43:272–277.
51. Fidler IJ, Brodey RS. The biological behavior of canine mammary neoplasms. *J Am Vet Med Assoc* 1967;151:1311–1318.
52. Verstegen J, Onclin K. Mammary tumors in the queen, in *Proceedings*. Annu Conf Soc Theriogenol 2003;239–245.
53. Dorn CR, Taylor DON, Frye FL, et al. Survey of animal neoplasms in Alameda and Contra Costa counties, California. I. Methodology and description of cases. *J Natl Cancer Inst* 1968; 40:295–305.
54. Moe L. Population-based incidence of mammary tumors in some dog breeds. *J Reprod Fertil Suppl* 2001;57:439–443.
55. Richards HG, McNeil PE, Thompson H, et al. An epidemiological analysis of a canine-biopsies database compiled by a diagnostic histopathology service. *Prev Vet Med* 2001;51:125–136.
56. Cotchin E. Neoplasms in small animals. *Vet Rec* 1951;63:67–72.
57. Brodey RS, Goldschmidt MH, Roszel JR. Canine mammary gland neoplasms. *J Am Anim Hosp Assoc* 1983;19:61–90.
58. Moulton JE, Taylor DON, Dorn CR, et al. Canine mammary tumors. *Pathol Vet* 1970;7:289–320.
59. Hampe JF, Misdorp W. Tumours and dysplasias of the mammary gland. *Bull World Health Organ* 1974;50:111–133.
60. Hayes HM, Milne KL, Mandel CP. Epidemiological features of feline mammary carcinoma. *Vet Rec* 1981;108:476–479.
61. Moulton JE, Rosenblatt LS, Goldman M. Mammary tumors in a colony of Beagle dogs. *Vet Pathol* 1986;23:741–749.
62. Misdorp W, Hart AAM. Canine mammary cancer. II. Therapy and causes of death. *J Small Anim Pract* 1979;20:395–404.
63. Cohen D, Reif JS, Brodey RS, et al. Epidemiological analysis of the most prevalent sites and types of canine neoplasia observed in a veterinary hospital. *Cancer Res* 1974;34:2859–2868.
64. Johnston SD, Root Kustritz MV, Olson PN. Disorders of the mammary glands of the bitch. In: Johnston SD, Root Kustritz MV, Olson PN, eds. *Canine and feline theriogenology*. Philadelphia: WB Saunders Co, 2001;246–253.
65. Sorenmo K. Canine mammary gland tumors. *Vet Clin North Am Small Anim Pract* 2003;33:573–596.
66. Misdorp W. Canine mammary tumours: protective effect of late ovariectomy and stimulating effect of progestins. *Vet Q* 1988;10:26–31.
67. Dorn CR, Taylor DON, Schneider R, et al. Survey of animal neoplasms in Alameda and Contra Costa counties, California. II. Cancer morbidity in dogs and cats from Alameda county. *J Natl Cancer Inst* 1968;40:307–318.
68. Schneider R, Dorn CR, Taylor DON. Factors influencing canine mammary cancer development and postsurgical survival. *J Natl Cancer Inst* 1969;43:1249–1261.
69. Verstegen J, Onclin K. Etiopathogeny, classification and prognosis of mammary tumors in the canine and feline species, in *Proceedings*. Annu Conf Soc Theriogenol 2003;230–238.
70. Donnay I, Rauis J, Devleeshouwer N, et al. Comparison of estrogen and progesterone receptor expression in normal and tumor mammary tissues from dogs. *Am J Vet Res* 1995;56:1188–1194.
71. Hamilton JM, Else RW, Forshaw P. Oestrogen receptors in canine mammary tumours. *Vet Rec* 1977;101:258–260.
72. Bell FW, Klausner JS, Hayden DW, et al. Clinical and pathologic features of prostatic adenocarcinoma in sexually intact and castrated dogs: 31 cases (1970–1987). *J Am Vet Med Assoc* 1991;199:1623–1630.
73. Weaver AD. Fifteen cases of prostatic carcinoma in the dog. *Vet Rec* 1981;109:71–75.
74. Teske E, Naan EC, VanDijk EM, et al. Canine prostate carcinoma: epidemiological evidence of an increased risk in castrated dogs. *Mol Cell Endocrinol* 2002;197:251–255.
75. Sorenmo KU, Goldschmidt M, Shofer F, et al. Immunohistochemical characterization of canine prostatic carcinoma and correlation with castration status and castration time. *Vet Comp Oncol* 2003;1:48–56.
76. Obradovich J, Walshaw R, Goulland E. The influence of castration on the development of prostatic carcinoma in the dog: 43 cases (1978–1985). *J Vet Intern Med* 1987;1:183–187.
77. Leav I, Ling GV. Adenocarcinoma of the canine prostate gland. *Cancer* 1968;22:1329–1345.
78. Durham SK, Dietze AE. Prostatic adenocarcinoma with and without metastases to bone in dogs. *J Am Vet Med Assoc* 1986; 188:1432–1436.
79. Lipowitz AJ, Schwartz AS, Wilson GP. Testicular neoplasms and concomitant clinical changes in the dog. *J Am Vet Med Assoc* 1973; 163:1364–1368.
80. Johnston SD, Root Kustritz MV, Olson PN. Testicular neoplasia. In: Johnston SD, Root Kustritz MV, Olson PN, eds. *Canine and feline theriogenology*. Philadelphia: WB Saunders Co, 2001;324–327.
81. Cotchin E. Neoplasia in the dog. *Vet Rec* 1954;66:879–888.
82. Brodey RS. Canine and feline neoplasia. *Adv Vet Sci Comp Med* 1970;14:309–354.
83. Johnston SD, Root Kustritz MV, Olson PN. Ovarian neoplasia. In: Johnston SD, Root Kustritz MV, Olson PN, eds. *Canine and feline theriogenology*. Philadelphia: WB Saunders Co, 2001;200–203, 459–461.
84. Johnston SD, Root Kustritz MV, Olson PN. Uterine neoplasia. In: Johnston SD, Root Kustritz MV, Olson PN, eds. *Canine and feline theriogenology*. Philadelphia: WB Saunders Co, 2001;221, 470.
85. Knapp DW, Glickman NW, DeNicola DB, et al. Naturally-occurring canine transitional cell carcinoma of the urinary bladder. *Urol Oncol* 2000;5:47–59.
86. Norris AM, Laing EJ, Valli VEO, et al. Canine bladder and urethral tumors: a retrospective study of 115 cases (1980–1985). *J Vet Intern Med* 1992;6:145–153.
87. Osborne CA, Low DG, Perman V, et al. Neoplasms of the canine and feline urinary bladder: incidence, etiologic factors, occurrence and pathologic features. *Am J Vet Res* 1968;29:2041–2055.
88. Tarvin G, Patnaik A, Greene R. Primary urethral tumors in dogs. *J Am Vet Med Assoc* 1978;172:931–933.
89. Poirier VJ, Forrest LJ, Adams WM, et al. Piroxicam, mitoxantrone, and coarse fraction radiotherapy for the treatment of transitional cell carcinoma of the bladder in 10 dogs: a pilot study. *J Am Anim Hosp Assoc* 2004;40:131–136.
90. Henry CJ. Management of the transitional cell carcinoma. *Vet Clin North Am Small Anim Pract* 2003;33:597–613.
91. Ru G, Terracini B, Glickman LT, et al. Related risk factors for canine osteosarcoma. *Vet J* 1998;156:31–39.
92. Cooley DM, Beranek BC, Schlittler DL, et al. Endogenous gonadal hormone exposure and bone sarcoma risk. *Canc Epidemiol Biomark Prev* 2002;11:1434–1440.
93. Chun R, DeLorimier L-P. Update on the biology and management of canine osteosarcoma. *Vet Clin North Am Small Anim Pract* 2003;33:491–516.
94. Colliard L, Ancel J, Benet JJ, et al. Risk factors for obesity in dogs in France. *J Nutr* 2006;136:1951S–1954S.
95. Priester WA, McKay FW. The occurrence of tumors in domestic animals. *Natl Cancer Inst Monogr* 1980;54:169.
96. Ware WA, Hopper DL. Cardiac tumors in dogs: 1982–1995. *J Vet Intern Med* 1999;13:95–103.
97. Smith AN. Hemangiosarcoma in dogs and cats. *Vet Clin North Am Small Anim Pract* 2003;33:533–552.
98. Prymak C, McKee LJ, Goldschmidt MH, et al. Epidemiologic, clinical, pathologic, and prognostic characteristics of splenic hemangiosarcoma and splenic hematoma in dogs: 217 cases (1985). *J Am Vet Med Assoc* 1988;193:706–712.
99. Shen V, Dempster DW, Birchman R, et al. Lack of changes in histomorphometric, bone mass, and biochemical parameters in ovariohysterectomized dogs. *Bone* 1992;13:311–316.
100. Ekici H, Sontas BH, Toydemir TSF, et al. The effect of prepubertal ovariohysterectomy on spine 1 mineral density and mineral content in puppies: a preliminary study. *Res Vet Sci* 2007;82:105–109.
101. Johnston SD, Root Kustritz MV, Olson PN. Prevention and termination of canine pregnancy. In: Johnston SD, Root Kustritz MV, Olson PN, eds. *Canine and feline theriogenology*. Philadelphia: WB Saunders Co, 2001;172.

102. Salmeri KR, Bloomberg MS, Scruggs SL, et al. Gonadectomy in immature dogs: effects on skeletal, physical and behavioral development. *J Am Vet Med Assoc* 1991;198:1193–1203.
103. Crenshaw WE, Carter CN. Should dogs in animal shelters be neutered early? *Vet Med* 1995;90:756–760.
104. Root MV, Johnston SD, Olson PN. The effect of prepuberal and postpuberal gonadectomy on radial physeal closure in male and female domestic cats. *Vet Radiol Ultrasound* 1997;38:42–47.
105. May C, Bennett D, Downham DY. Delayed physeal closure associated with castration in cats. *J Small Anim Pract* 1991;32:326–328.
106. Houlton JEF, McGlennon NJ. Castration and physeal closure in the cat. *Vet Rec* 1992;131:466–467.
107. McNicholas WT, Wilkens BE, Blevins WE, et al. Spontaneous femoral capital physeal fractures in adult cats: 26 cases (1996–2001). *J Am Vet Med Assoc* 2002;221:1731–1736.
108. Keller GG, Corley EA. Canine hip dysplasia: investigating the sex predilection and the frequency of unilateral CHD. *Vet Med* 1989;Dec:1162–1166.
109. Kealy RD, Olsson SE, Monti KL, et al. Effects of limited food consumption on the incidence of hip dysplasia in growing dogs. *J Am Vet Med Assoc* 1992;201:857–863.
110. Kaneene JB, Mostosky UV, Padgett GA. Retrospective cohort study of changes in hip joint phenotype of dogs in the United States. *J Am Vet Med Assoc* 1997;211:1542–1544.
111. Ledecky V, Sevcik A, Puzder M, et al. Occurrence of hip joint dysplasia in some hunting breeds. *Vet Archiv* 2004;74:417–425.
112. Priester WA, Mulvihill JJ. Canine hip dysplasia: relative risk by sex, size, and breed, and comparative aspects. *J Am Vet Med Assoc* 1972;160:735–739.
113. Arendt EA. Orthopaedic issues for active and athletic women. *Clin Sports Med* 1994;13:483–503.
114. Harasen G. Canine cranial cruciate ligament rupture in profile. *Can Vet J* 2003;44:845–846.
115. Duval JM, Budsberg SC, Flo GL, et al. Breed, sex, and body weight as risk factors for rupture of the cranial cruciate ligament in young dogs. *J Am Vet Med Assoc* 1999;215:811–814.
116. Whitehair JG, Vasseur PB, Willits NH. Epidemiology of cranial cruciate ligament rupture in dogs. *J Am Vet Med Assoc* 1993;203:1016–1019.
117. Slauterbeck JR, Pankratz K, Xu KT, et al. Canine ovariohysterectomy and orchiectomy increases the prevalence of ACL injury. *Clin Orthop* 2004;429:301–305.
118. Wilke VL, Conzemius MG, Kinghorn BP, et al. Inheritance of rupture of the cranial cruciate ligament in Newfoundlands. *J Am Vet Med Assoc* 2006;228:61–64.
119. Mason E. Obesity in pet dogs. *Vet Rec* 1970;86:612–616.
120. Edney ATB, Smith PM. Study of obesity in dogs visiting veterinary practices in the United Kingdom. *Vet Rec* 1986;118:391–396.
121. Sloth C. Practical management of obesity in dogs and cats. *J Small Anim Pract* 1992;33:178–182.
122. Crane SW. Occurrence and management of obesity in companion animals. *J Small Anim Pract* 1991;32:275–282.
123. Flynn MF, Hardie EM, Armstrong PJ. Effect of ovariohysterectomy on maintenance energy requirement in cats. *J Am Vet Med Assoc* 1996;209:1572–1581.
124. Martin LJM, Siliart B, Dumon HJW, et al. Spontaneous hormonal variations in male cats following gonadectomy. *J Feline Med Surg* 2006;8:309–314.
125. Fettman MJ, Stanton CA, Banks LL, et al. Effects of neutering on body weight, metabolic rate and glucose tolerance of domestic cats. *Res Vet Sci* 1997;62:131–136.
126. Root MV, Johnston SD, Olson PN. Effect of prepuberal and postpuberal gonadectomy on heat production measured by indirect calorimetry in male and female domestic cats. *Am J Vet Res* 1996;57:371–374.
127. Nguyen PG, Dumon HJ, Siliart BS, et al. Effects of dietary fat and energy on body weight and composition after gonadectomy in cats. *Am J Vet Res* 2004;65:1708–1713.
128. British Small Animal Veterinary Association. Sequelae of bitch sterilisation: regional survey. *Vet Rec* 1975;96:371–372.
129. Houpt KA, Coren B, Hintz HF, et al. Effect of sex and reproductive status on sucrose preference, food intake, and body weight of dogs. *J Am Vet Med Assoc* 1979;174:1083–1085.
130. Robertson ID. The association of exercise, diet and other factors with owner-perceived obesity in privately owned dogs from metropolitan Perth, WA. *Prev Vet Med* 2003;58:75–83.
131. Seguin MA, Vaden SL, Altier C, et al. Persistent urinary tract infections and reinfections in 100 dogs (1989–1999). *J Vet Intern Med* 2003;17:622–631.
132. Root MV, Johnston SD, Johnston GR, et al. The effect of prepuberal and postpuberal gonadectomy on penile extrusion and urethral diameter in the domestic cat. *Vet Radiol Ultrasound* 1996;37:363–366.
133. Herron MA. A potential consequence of prepuberal feline castration. *Feline Pract* 1971;1:17–19.
134. Senior D. Lower urinary tract disease—feline, in *Proceedings*. World Small Anim Vet Assoc Cong 2006. Available at: www.vin.com/proceedings/Proceedings.plx?CID=WSAVA2006&PID=16089&O=Generic. Accessed Jun 2, 2007.
135. Herron MA. The effect of prepubertal castration on the penile urethra of the cat. *J Am Vet Med Assoc* 1972;160:208–211.
136. Lekcharoensuk C, Osborne CA, Lulich JP. Epidemiologic study of risk factors for lower urinary tract diseases in cats. *J Am Vet Med Assoc* 2001;218:1429–1435.
137. Holt PE. Urinary incontinence in the male and female dog or does sex matter? Available at: www.vin.com. Accessed Oct 1, 2004.
138. Angioletti A, DeFrancesco I, Vergottini M, et al. Urinary incontinence after spaying in the bitch: incidence and oestrogen therapy. *Vet Res Commun* 2004;28(suppl 1):153–155.
139. Stocklin-Gautschi NM, Hassig M, Reichler IM, et al. The relationship of urinary incontinence to early spaying in bitches. *J Reprod Fertil* 2001;(suppl 57):233–236.
140. Arnold S. Urinary incontinence in castrated bitches. Part I. Significance, clinical aspects and etiopathogenesis. *Schweiz Arch Tierheilkd* 1997;139:271–276.
141. Thrusfield MV, Holt PE, Muirhead RH. Acquired urinary incontinence in bitches: its incidence and relationship to neutering practices. *J Small Anim Pract* 1998;39:559–566.
142. Holt PE, Thrusfield MV. Association in bitches between breed, size, neutering and docking, and acquired urinary incontinence due to incompetence of the urethral sphincter mechanism. *Vet Rec* 1993;133:177–180.
143. Gregory SP, Parkinson TJ, Holt PE. Urethral conformation and position in relation to urinary incontinence in the bitch. *Vet Rec* 1992;131:167–170.
144. Gregory SP, Holt PE, Parkinson TJ, et al. Vaginal position and length in the bitch: relationship to spaying and urinary incontinence. *J Small Anim Pract* 1999;40:180–184.
145. Atalan G, Holt PE, Barr FJ. Ultrasonographic assessment of bladder neck mobility in continent bitches and bitches with urinary incontinence attributable to urethral sphincter mechanism incompetence. *Am J Vet Res* 1998;59:673–679.
146. Beijerink NJ, Buijtels JJCWM, Okkens AC, et al. Basal and GnRH-induced secretion of FSH and LH in anestrous versus ovariectomized bitches. *Theriogenology* 2007;67:1039–1045.
147. Reichler IM, Pfeiffer E, Piche CA, et al. Changes in plasma gonadotropin concentrations and urethral closure pressure in the bitch during the 12 months following ovariectomy. *Theriogenology* 2004;62:1391–1402.
148. Reichler IM, Hung E, Jochle W, et al. FSH and LH plasma levels in bitches with differences in risk for urinary incontinence. *Theriogenology* 2005;63:2164–2180.
149. Reichler IM, Hubler M, Jochle W, et al. The effect of GnRH analogs on urinary incontinence after ablation of the ovaries in dogs. *Theriogenology* 2003;60:1207–1216.
150. Reichler IM, Welle M, Sattler U, et al. Comparative quantitative assessment of GnRH- and LH-receptor mRNA expression in the urinary tract of sexually intact and spayed female dogs. *Theriogenology* 2007;67:1134–1142.
151. Rosenthal KL, Peterson ME, Quesenberry KE, et al. Hyperadrenocorticism associated with adrenocortical tumor or nodular hyperplasia of the adrenal gland in ferrets: 50 cases (1987–1991). *J Am Vet Med Assoc* 1993;203:271–275.
152. Shoemaker NJ, Schuurmans M, Moorman H, et al. Correlation

between age at neutering and age at onset of hyperadrenocorticism in ferrets. *J Am Vet Med Assoc* 2000;216:195–197.
153. Olson PN. Early spay and neuter, in *Proceedings*. North Am Vet Conf 1997;25.
154. Johnson-Delaney CA. Ferret adrenal disease: 2006 perspective. *Exotic DVM* 2006;8:31–34.
155. Pabon JE, Li X, Lei ZM, et al. Novel presence of luteinising hormone/chorionic gonadotropin receptors in human adrenal glands. *J Clin Endocrinol Metab* 1996;81:2397–2400.
156. Schoemaker NJ, Teerds KJ, Mol JA, et al. The role of luteinizing hormone in the pathogenesis of hyperadrenocorticism in neutered ferrets. *Mol Cell Endocrinol* 2002;197:117–125.
157. Fukuda S. Incidence of pyometra in colony-raised Beagle dogs. *Exp Anim* 2001;50:325–329.
158. Egenvall A, Hagman R, Bonnett BN, et al. Breed risk of pyometra in insured dogs in Sweden. *J Vet Intern Med* 2001;15:530–538.
159. Niskanen M, Thursfield MV. Associations between age, parity, hormonal therapy and breed, and pyometra in Finnish dogs. *Vet Rec* 1998;143:493–498.
160. Potter K, Hancock DH, Gallina AM. Clinical and pathologic features of endometrial hyperplasia, pyometra, and endometritis in cats: 79 cases (1980–1985). *J Am Vet Med Assoc* 1991;198:1427–1431.
161. Johnston SD, Root Kustritz MV, Olson PN. Disorders of the canine uterus and uterine tubes (oviducts). In: Johnston SD, Root Kustritz MV, Olson PN, eds. *Canine and feline theriogenology*. Philadelphia: WB Saunders Co, 2001;216.
162. Johnston SD, Root Kustritz MV, Olson PN. Disorders of the feline uterus and uterine tubes (oviducts). In: Johnston SD, Root Kustritz MV, Olson PN, eds. *Canine and feline theriogenology*. Philadelphia: WB Saunders Co, 2001;468.
163. O'Shea JD. Studies on the canine prostate gland. I. Factors influencing its size and weight. *J Comp Pathol* 1962;72:321–331.
164. Zirkin BR, Strandberg JD. Quantitative changes in the morphology of the aging canine prostate. *Anat Rec* 1984;208:207–214.
165. Mackenzie AR, Hall T, Lo M-C, et al. Influence of castration and sex hormones on size, histology and zinc content of canine prostate. *J Urol* 1963;89:864–874.
166. Lowseth LA, Gerlach RF, Gillett NA, et al. Age-related changes in the prostate and testes of the Beagle dog. *Vet Pathol* 1990;27:347–353.
167. Berry SJ, Strandberg JD, Saunders WJ, et al. Development of canine benign prostatic hyperplasia with age. *Prostate* 1986;9:363–373.
168. Dorfman M, Barsanti J. Diseases of the canine prostate gland. *Compend Contin Educ Pract Vet* 1995;17:791–810.
169. Cowan LA, Barsanti JA, Crowell W, et al. Effects of castration on chronic bacterial prostatitis in dogs. *J Am Vet Med Assoc* 1991;199:346–350.
170. Johnston SD, Root Kustritz MV, Olson PN. Disorders of the canine prostate. In: Johnston SD, Root Kustritz MV, Olson PN, eds. *Canine and feline theriogenology*. Philadelphia: WB Saunders Co, 2001;340.
171. Hess RS, Kass PH, Ward CR. Breed distribution of dogs with diabetes mellitus admitted to a tertiary care facility. *J Am Vet Med Assoc* 2000;216:1414–1417.
172. Marmor M, Willeberg P, Glickman LT, et al. Epizootiologic patterns of diabetes mellitus in dogs. *Am J Vet Res* 1982;43:465–470.
173. McCann TM, Simpson KE, Shaw DJ, et al. Feline diabetes mellitus in the UK: the prevalence within an insured cat population and a questionnaire-based putative risk factor analysis. *J Feline Med Surg* 2007;9:289–299.
174. Prahl A, Guptill L, Glickman NW, et al. Time trends and risk factors for diabetes mellitus in cats presented to veterinary teaching hospitals. *J Feline Med Surg* 2007;[E-pub ahead of print]. doi:10.1016/j.jfms.2007.02.004.
175. Rand JS, Bobbermien LM, Hendrikz JK, et al. Over representation of Burmese cats with diabetes mellitus. *Aust Vet J* 1997;75:402–405.
176. Panciera DL. Hypothyroidism in dogs: 66 cases (1987–1992). *J Am Vet Med Assoc* 1994;204:761–767.
177. Milne KL, Hayes HM. Epidemiological features of canine hypothyroidism. *Cornell Vet* 1981;71:3–14.
178. National Center for Health Statistics. *Health, United States 2006: with chartbook on trends in the health of Americans*. Hyattsville, Md: National Center for Health Statistics, 2006;176.
179. Moore GE, Burkman KD, Carter MN, et al. Causes of death or reasons for euthanasia in military working dogs: 927 cases (1993–1996). *J Am Vet Med Assoc* 2001;219:209–214.
180. Bronson RT. Variation in age at death of dogs of different sexes and breeds. *Am J Vet Res* 1982;43:2057–2059.
181. Michell AR. Longevity of British breeds of dog and its relationship with sex, size, cardiovascular variables and disease. *Vet Rec* 1999;145:625–629.
182. Greer KA, Canterberry SC, Murphy KE. Statistical analysis regarding the effects of height and weight on life span of the domestic dog. *Res Vet Sci* 2007;82:208–214.
183. Robertson OH. Prolongation of the life span of Kokanee salmon (*Oncorhynchus nerka kennerly*) by castration before beginning of gonad development. *Proc Natl Acad Sci U S A* 1961;47:609–621.