Reproduction in Domestic Animals

Reprod Dom Anim **47** (Suppl. 4), 214–222 (2012); doi: 10.1111/j.1439-0531.2012.02078.x ISSN 0936-6768

Effects of Surgical Sterilization on Canine and Feline Health and on Society

MV Root Kustritz

University of Minnesota College of Veterinary Medicine, St. Paul, MN, USA

Contents

Surgical sterilization of dogs and cats is a well-accepted measure for population control in some countries, but is considered unethical as an elective surgery in other countries. This is a review of what is known regarding positive and negative effects of gonadectomy surgery on individual animals and on societal management of unowned dog and cat populations.

Introduction

Elective gonadectomy, castration in males and either ovariectomy (OV) or ovariohysterectomy (OHE) in females, is the most common small animal surgery performed in some countries and is unethical or illegal in other countries (Salmeri et al. 1991b; Gunzel-Apel 1998; Greenfield et al. 2004). There is no question that we alter animals when we perform gonadectomy. This is a review of the specific changes associated with gonadectomy in dogs and cats and the evidence we have for cause-and-effect. Thorough reviews of the literature have been published (Root Kustritz 2007, 2010; Reichler 2009).

Some recognized reasons for the promotion of gonadectomy and some stated concerns are societal in nature, some refer to populations of animals, and some are pertinent to health of individual animals. Veterinarians are encouraged to help clients and those who write public policy to understand which aspect is being addressed when specific recommendations for gonadectomy are being made. There also is great variability in number of studies supporting some of the findings described, and veterinarians are encouraged to be aware of the amount of evidence to support any given claim. Finally, breed predispositions exist for some of the concerns described and must be included in decisions about suitability of gonadectomy in a given animal.

Advantages of gonadectomy include decrease in reproductive tract disease, including pyometra and mammary neoplasia in bitches and queens, and testicular neoplasia and prostate disease in male dogs. Other advantages include: decrease in pregnancy and parturition-related disorders including metritis, mastitis and dystocia; decrease in hormone-associated disorders such as vaginal prolapse in bitches and mammary hypertrophy in queens; and decrease in undesirable sexual behaviours (Romagnoli 2008). Disadvantages of gonadectomy include surgical and anaesthetic complications, increased risk of neoplasia of various organ systems, increased incidence of some musculoskeletal and endocrinologic disorders, obesity and urinary incontinence in bitches. All of these will be described in more detail. This discussion incorporates early spay-neuter, defined as gonadectomy at 8–16 weeks of age (Root Kustritz 1999), and gonadectomy at any age after 16 weeks.

Surgical and Anaesthetic Risk

General recommendations for anaesthesia are to minimize anaesthetic dose and time under anaesthesia. A series of excellent studies evaluating morbidity and mortality of dogs and cats identified general risk factors and some specific risk factors that are easily countered (Brodbelt et al. 2008; Brodbelt 2009, 2010). Cats were at greater risk of morbidity or mortality than dogs because of difficulties with intubation and prevalence of inapparent cardiomyopathy. If 6 months to 5 years of age is set as a baseline, all other ages were at greater risk, with a slight risk for younger animals and much greater risk for geriatric animals. Hypothermia greatly increased risk of morbidity or mortality during an anaesthetic episode. Profound hypothermia may develop as early as during induction and surgery prep. Body temperature should be monitored regularly and external sources of heat applied as needed. All animals, especially very young animals, should be weighed to ensure overdosing of drugs does not occur. Intra-operative monitoring shown to be of great benefit included recording of body temperature, pain assessment and use of pulse oximetry.

Concerns about anaesthesia are most commonly voiced when considering gonadectomy of very young animals. Concerns specific to animals < 4–5 months of age include altered ability to metabolize and excrete anaesthetic agents and pain medication because of immature renal and hepatic function, decreased protein binding of medications in the bloodstream, predisposition to hypoglycaemia because of decreased gluconeogenesis and minimal glycogen stores in skeletal muscle, and decreased ability to maintain body temperature (Root Kustritz 1999). Puppies and kittens < 10 weeks of age should be fasted for no more than 3-4 h before surgery and older animals fasted for no more than 8 h (Faggella and Aronsohn 1993, 1994). All surgical preparation fluids should be warmed and clipping of hair kept to a minimum. In studies of 98 puppies and 98 kittens presented for elective gonadectomy, incidence of anaesthetic complications was 0% for both groups (Aronsohn and Faggella 1993; Faggella and Aronsohn 1994). When looking at anaesthetic complications for gonadectomy at all ages, cardiac dysrhythmias, gastric dilation and drug overdosage were identified as the most common anaesthetic complications (Howe 1997).

Intra-operative and post-surgical complications are reported usually to be mild and self-limiting. Reported incidence of surgical complications is 6.1–27% in bitches

and dogs and 2.6–33% in queens and toms (Pollari et al. 1996; Romagnoli 2008). The wide range reported most likely is due to differing definitions of 'complications' in the papers cited. Most post-surgical complications are reported to be mild, with most requiring only nursing care and not veterinary intervention. Incidence of complications is lower in young animals than in older animals, with one study identifying fewer complications in animals gonadectomized prepuberally and another study identifying 2 years of age as a cut-off (Faggella and Aronsohn 1994; Pollari et al. 1996; Howe 1997; Romagnoli 2008).

Reported short-term complications of OV or OHE include haemorrhage of the ovarian or uterine pedicle, passage of bloody vulvar discharge, onset of pseudocyesis, dehiscence or infection of the incision and, very rarely, peritonitis or evisceration (Romagnoli 2008). Long-term complications of OV or OHE include ovarian remnant syndrome, ligation of a ureter with subsequent hydroureter and ipsilateral renal dysfunction, granuloma of the uterine or ovarian pedicle, and disease of the uterine stump (Romagnoli 2008). Reported incidence of complications is not correlated with age of the animal, ability of the surgeon or presence of reproductive disease (Miller 1995; Romagnoli 2008). Complications associated with haemorrhage may be more common when bitches and queens are spayed while in oestrus under the influence of oestrogen, and increased incidence of complications is associated with increased surgery time and increased body weight of the patient (Howe 1997; Howe et al. 2000, 2001; Burrow et al. 2005).

Population Control

Pet overpopulation may occur due to attitudes of the animal owning public permitting irresponsible breeding or ready surrender of animals or due to free-roaming or feral dogs and cats. Although it has been reported that 82% of cats and 64% of dogs in the US have undergone gonadectomy (Trevejo et al. 2011), a recent study reported that only 52% of people who had purchased a dog or cat within the last year had had that animal gonadectomized (PetSmart Charities 2002). In the United States, millions of dogs and cats with no owner or guardian are euthanized annually (Nassar et al. 1992; National Council on Pet Population Study and Policy 1994). Intact animals are more likely to be surrendered to humane organizations (Patronek et al. 1996a,b; New et al. 2000; Mondelli et al. 2004). Spay-neuter contracts are sent out with animals adopted while still intact but compliance with these contracts, even with low-cost surgical options readily available, is <60%, permitting intact animals to re-populate those shelters from which they were adopted (Alexander and Shane 1994; Patronek et al. 1996a; New et al. 2000; Mondelli et al. 2004). Lack of compliance with recommendations for surgery is multifactorial. Cultural and personal factors include religious affiliation, ethnic background, intended working life of the animal, urban or rural location of the household and literacy status (Manning and Rowan 1992; Mahlow 1999; Eze and Eze 2002). Cats are more likely to be spayed or castrated than are dogs, and females are more likely to be presented for gonadectomy than are males in the United States (Manning and Rowan 1992; Alexander and Shane 1994; Mahlow 1999; New et al. 2000).

Many pet owners have limited knowledge about normal reproduction in dogs and cats. In the PetSmart survey (PetSmart Charities A&U Barriers 2002), 13% of dogs and 19% of cats purchased within the previous year had borne litters, with over 50% of those unplanned. In one survey of dog- and cat-owning households, 56% of 154 canine litters and 68% of 317 feline litters were unplanned, with the majority of those owners reporting that they did not know the female had been in heat (New et al. 2004). Because of this, many humane organizations in the United States are working toward gonadectomy of all unowned animals prior to adoption. Other measures that will be required to stem pet overpopulation include education of pet owners and increased availability of affordable, safe, readily provided non-surgical contraceptive or sterilization options.

Behaviour

Many people request gonadectomy because they are unwilling or unable to tolerate normal breeding behaviours in their animals. Male cat normal breeding behaviour, which is aggressive and includes urine spraying, is incompatible with life as a house pet (Root Kustritz 1996). Male dogs may mount other animals, people or inanimate objects and may urine mark. Bitches and queens may show altered behaviours with oestrus, including increases in some forms of aggression, and bitches may show nesting and mothering behaviours and lactation with false pregnancy.

Gonadectomy, especially castration, is a commonly recommended treatment for behavioural problems in dogs including aggression. Not all behaviours are altered by gonadectomy. Those most commonly affected are sexually dimorphic behaviours, defined as behaviours that vary between genders, and are likely to be at least partially mediated by sex hormones.

In male cats, the undesirable behaviours decreased to the greatest extent by castration are sexual behaviours, roaming and urine spraying (Hart 1973, 1979; Hart and Barrett 1973). In male dogs, the undesirable behaviours decreased to the greatest extent by castration are mounting, urine marking and roaming (Hart 1979; Neilson et al. 1997). Likelihood of response to castration is not associated with age at castration or duration of the behaviour prior to castration in male dogs or cats (Hart 1973; Hart and Barrett 1973; Hopkins et al. 1976; Neilson et al. 1997). The hormonal basis of these behaviours is not always clear. Oestrogen stimulates arousal in females but also is associated with release of oxytocin and opioids, which may have an anti-anxiety effect (Mong and Pfaff 2003; Root Kustritz 2005). Concerns vary regarding trainability of dogs after gonadectomy, with some suggesting that dogs will be more attentive after gonadectomy as they are less likely to show behaviours related to copulation, such as roaming. It has been demonstrated in rats that attention is not affected by rising or falling concentrations of testosterone, but that acuity of spatial working memory

is testosterone dependent (Johnson and Burk 2006; Kritzer et al. 2007).

Aggression may or may not be affected by gonadectomy (Hart and Eckstein 1997; Neilson et al. 1997; Duffy and Serpell 2006). A breed-specific increase in owner-directed aggression and in degree of reactivity was reported in both males and females after gonadectomy and in bitches after OHE; in one study, this increase in aggression was most common in bitches spayed at < 1 year of age who were showing aggression prior to surgery (Wright and Nesselrote 1987: O'Farrell and Peachey 1990; Reisner et al. 2005; Duffy and Serpell 2006). The form of aggression best controlled by castration in both male dogs and cats is intermale aggression (Hart 1979; Borchelt and Voith 1987). Other forms of aggression in cats include predation, play, fear or defence, territorial and redirected aggression; these are much less likely to be decreased by castration (Borchelt 1983). Other forms of aggression in dogs include predation, fear or defence, dominance, protectiveness, punishment and pain-related aggression (Borchelt 1983).

In one study of older male dogs with mild cognitive impairment, those that were castrated were more likely to progress to severe cognitive impairment than were those left intact (Hart 2001). Androgen deprivation is associated increased deposition of amyloid in brains of humans and rodents and with decreased number of synaptic connections in brains of rodents and primates (Janowsky 2006). However, studies directly evaluating the brain of aged dogs showed that among beagles aged approximately 10 years, intact dogs had more DNA damage in the brain than did castrated dogs (Waters et al. 2000).

Neoplasia

Mammary

Mammary neoplasia is very common in dogs and cats, with reported incidence of 3.4 and 2.5%, respectively, in the United States (Fidler and Brodey 1967; Dorn et al. 1968a; Moe 2001; Richards et al. 2001; Verstegen and Onclin 2003a). In dogs, approximately half of all mammary tumours are malignant; in cats, >90% of mammary tumours are malignant (Cotchin 1951; Dorn et al. 1968a; Moulton et al. 1970; Hampe and Misdorp 1974; Hayes et al. 1981; Brodey et al. 1983). Despite the fact that many mammary tumours in bitches are benign, it was reported in one U.S. study that 59.7% of bitches with mammary neoplasia were euthanized at the time of diagnosis (Misdorp and Hart 1979). It has been well demonstrated that incidence of mammary cancer when aged is greatly decreased in female dogs and cats by ovariectomy, especially if performed before the first heat cycle. Intact dogs and cats are seven times more likely than are spayed dogs and cats to develop mammary neoplasia when aged (Dorn et al. 1968b). Risk for bitches has been defined as 0.5% before the first oestrus, 8% after one oestrus, and 26% after two or more oestrous cycles (Schneider et al. 1969). Some sparing effect may be present with OHE up to 9 years of age. although that effect may be greater for benign than for malignant tumours (Verstegen and Onclin 2003b; Reichler 2009). Siamese cats and Japanese domestic breed cats are reported to be at greater risk of developing mammary neoplasia, as are the boxer, Brittany spaniel, cocker spaniel, dachshund, English setter, English springer spaniel, German shepherd dog, Maltese, miniature poodle, pointer, toy poodle and Yorkshire terrier (Dorn et al. 1968b; Hayes et al. 1981; Sorenmo 2003; Verstegen and Onclin 2003a). Causeand-effect relationship between gonadectomy and decreased incidence of mammary neoplasia is not clear. In human medicine, oestrogen is implicated in mammary neoplasia. Oestrogen receptors have been identified in neoplastic mammary tissue of dogs and cats, with fewer oestrogen receptors present as tissue becomes more anaplastic (Hamilton et al. 1977; Donnay et al. 1995; Verstegen and Onclin 2003b). One study suggested that mammary neoplasia may be more common in bitches that exhibited more than three episodes of overt false pregnancy in their lives, again supporting a role for hormonal stimulation of mammary tissue as a factor associated with neoplastic transformation of that tissue (Verstegen and Onclin 2003b).

Genitourinary

Prostate

Prostatic neoplasia is uncommon in dogs, with reported incidence of 0.2–0.6% (Bell et al. 1991; Teske et al. 2002). Prostatic neoplasia in dogs virtually always is malignant; both adenocarcinoma and transitional cell carcinoma are described. Several studies have documented increased incidence of prostatic cancer in castrated dogs compared with intact dogs, with reported increased risk ranging from 2.4 to 4.3 times (Obradovich et al. 1987; Bell et al. 1991; Teske et al. 2002; Sorenmo et al. 2003). Prostatic neoplasia is extremely uncommon in cats, but in one case series of eight cats with prostatic neoplasia, seven were castrated (Hawe 1983; Carpenter et al. 1987; Hubbard et al. 1990; Caney et al. 1998; LeRoy and Lech 2004). No breed predisposition is reported. Cause-and-effect relationship is not clear.

Urinary bladder

Incidence of transitional cell carcinoma is at most 1% of malignant tumours (Poirier et al. 2004). Incidence of transitional cell carcinoma of the urinary bladder and urethra of female dogs and urethra of male dogs is reported to be increased after gonadectomy, with increased risk of 2–4 times (Norris et al. 1992; Knapp et al. 2000). This has not been reported in cats. Dog breeds at increased risk are the Airedale terrier, beagle, collie, Scottish terrier, Shetland sheepdog, West Highland white terrier and wire-haired fox terrier (Ru et al. 1998). Cause-and-effect relationship is not clear.

Testicular

Testicular neoplasia is very common in aged male dogs, with reported incidence of 0.9% (Hahn et al. 1992). The three tumour types most commonly reported are Sertoli

cell tumours, seminomas and Leydig (interstitial) cell tumours. Testicular neoplasia is uncommon in male cats. Castration is curative.

Haematologic

Overall incidence of haemangiosarcoma in dogs is 0.2% and in cats is 0.03% (Reichler 2009). Incidence of both splenic- and heart-based haemangiosarcoma are reported to be increased in dogs after gonadectomy; in bitches, splenic haemangiosarcoma risk after OHE increases by a factor of 2.2 and cardiac haemangiosarcoma risk increases by a factor of 5, and in male dogs, overall risk of haemangiosarcoma increases by a factor 2.4 after castration (Prymak et al. 1988; Ware and Hopper 1999). This has not been reported in cats. Breeds at increased risk are the boxer, English setter, German shepherd dog, golden retriever, Great Dane, Labrador retriever, pointer, poodle and Siberian husky (Smith 2003). Cause-and-effect relationship is not clear.

Orthopaedic

Osteosarcoma is an uncommon tumour with overall incidence of 0.2% (Root Kustritz 2007). Incidence is increased with gonadectomy, by a factor of 1.3–2 (Priester and McKay 1980; Ru et al. 1998). Breeds at increased risk are the Doberman pinscher, Great Dane, Irish setter, Irish wolfhound, rottweiler and St. Bernard (Ru et al. 1998; Chun and DeLorimer 2003). Other risk factors for osteosarcoma include increasing age and increasing body weight (Ru et al. 1998; Cooley et al. 2002). Cause-and-effect relationship is not clear.

Dermatologic

Increase incidence of cutaneous mast cells tumours has been reported in spayed female dogs compared with intact female dogs (White et al. 2011). Cause-and-effect relationship is not clear.

Musculoskeletal Disease

Growth plate closure

Growth plate closure in long bones is mediated by gonadal hormones. It has been well demonstrated that growth plate closure is delayed in dogs and cats spayed or castrated prepuberally (May et al. 1991; Salmeri et al. 1991a; Houlton and McGlennon 1992; Root et al. 1996c; Stubbs et al. 1996). Significance of this delay is not clear. Increased incidence of growth plate fractures in cats spayed prepuberally was demonstrated in one study; obesity may have contributed to the disorder in those cats (McNicholas et al. 2002).

Hip dysplasia

One large study evaluating incidence of various disorders in dogs spayed at various ages in a humane organization reported increased incidence of hip dysplasia in dogs spayed when young (Spain et al. 2004b). It was not clear in that study that all dogs were

diagnosed with hip dysplasia by a veterinarian. In one study, it was demonstrated that neutered boxers were 1.5 times as likely as intact boxers to develop hip dysplasia; that study did not figure in possible contribution of excess body weight (VanHagen et al. 2005). Hip dysplasia has a strong genetic component. Breeds at risk include the Chesapeake Bay retriever, English setter, German shepherd dog, golden retriever, Labrador retriever, Samoyed and St. Bernard (Priester and Mulvihill 1972). A hypothesis for cause-and-effect is asymmetry in closure of growth plates causing deformity and laxity of the hip joint with subsequent arthritis.

Anterior Cruciate Ligament (ACL) Rupture

Rupture of the anterior or cranial cruciate ligament is more common after gonadectomy than in intact dogs (Whitehair et al. 1993; Duval et al. 1999; Slauterbeck et al. 2004). Breeds at risk for rupture of the ACL include the Akita, American Staffordshire terrier, Chesapeake Bay retriever, German shepherd dog, golden retriever, Labrador retriever, mastiff, Neopolitan mastiff, Newfoundland, poodle, rottweiler and St. Bernard (Duval et al. 1999; Harasen 2003). Other risk factors include obesity and abnormal angulation of the stifle (Ragetly et al. 2011). One could argue that increased risk of ACL injury after gonadectomy is because of decreased athleticism and obesity in gonadectomized animals but the trend stands even in studies that statistically compensated for these effects in dogs. Joint laxity may differ under varying hormonal stimuli, suggesting one possible cause-and-effect mechanism. Another hypothesis is increasing stifle angulation with asymmetry of growth plate closure in the femur and tibia.

Genitourinary Disease

Urinary incontinence

Urethral sphincter mechanism incompetence, formerly called oestrogen-responsive urinary incontinence, is leakage of urine from female dogs, usually as they lie relaxed. A similar clinical manifestation is seen in castrated male dogs but is less common than in females. Urethral sphincter mechanism incompetence is much more common in spayed than in intact female dogs with reported incidence of 4.9–20.0% (Arnold 1997; Stocklin-Gautschi et al. 2001; Angioletti et al. 2004; Spain et al. 2004b). One study identified 3 months of age as the age before which OHE most greatly contributed to eventual clinical manifestation of urinary incontinence (Spain et al. 2004b). Other contributing factors include higher lean body weight (>20 kg); breed, with breeds at increased risk including the boxer, Doberman pinscher, giant schnauzer, Irish setter, old English sheepdog, rottweiler, springer spaniel and Weimeraner; and urethral length or resting position of the urinary bladder creating a pressure differential across the length of the urethra (Gregory et al. 1992, 1999; Holt and Thursfield 1993; Arnold 1997; Atalan et al. 1998; Holt 2004). Urethral sphincter tone is mediated by the sympathetic nervous system and function may be potentiated by

oestrogen. Cause-and-effect for urinary incontinence after OHE has not been identified. Hypothesized causes include physical factors, alteration in gonadotropin secretion after OHE, and change in muscle tone (Ponglowhapan et al. 2008a,b, 2011).

Pyometra

Incidence of pyometra in dogs left intact is high, at 24–25% by 10 years of age (Hagman et al. 2011). Pyometra also occurs in cats, even in those queens not known to have been induced to ovulate (Potter et al. 1991). Although OHE is considered curative, morbidity is relatively high and mortality with surgical management is 0–17% in dogs and 8% in cats (Johnston et al. 2001a,b).

Benign prostatic hypertrophy

Benign prostatic hyperplasia is very common in aged dogs, with reported incidence of 50% by 2.4 years of age and 75–80% in dogs aged 6 years or more (Zirkin and Strandberg 1984; Berry et al. 1986; Lowseth et al. 1990). BPH is not reported in cats. Castration is curative.

Disorders of the lower urinary tract

Multiple studies have failed to show any correlation between castration, urethral diameter, and incidence of urinary tract obstruction in male cats (Foster 1967; Herron 1972; Duch et al. 1978; Root et al. 1996a; Spain et al. 2004a). The balanopreputial fold, a tissue that connects the penile and preputial mucosa in early embryonic development, is androgen dependent. The fold undergoes dissolution as serum testosterone concentrations rise. In male cats, it has been demonstrated that at 12-22 months of age, 0-100% of cats castrated before 7 weeks of age could extrude their penis from the prepuce, whereas 40–100% of cats castrated at 7 months of age were capable of complete penile extrusion (Herron 1972; Root et al. 1996a; Stubbs et al. 1996). Clinical significance of inability to extrude the penis is unclear. Similarly, dogs castrated at <7 weeks of age had smaller penile diameter, decreased size and radiodensity of the os penis, and immature preputial development compared with male dogs castrated at 7 months of age or left intact (Salmeri et al. 1991a). Again, clinical significance is unclear.

Endocrinologic Disease

Adrenal Disease

In ferrets in the United States, most of which are spayed or castrated prepuberally, there is increased incidence of adrenocortical tumours and nodular adrenal hyperplasia (Lawrence et al. 1993; Rosenthal et al. 1993). The hypothesis is that lack of down-regulation of sex steroids or increased blood concentrations of gonadotropins cause adrenal gland hyperplasia and neoplastic transformation (Babon et al. 1996; Schoemaker et al. 2002; Johnson-Delaney 2006). However, in one survey

of 100 proliferative adrenal lesions in ferrets, almost 30% were from intact jills (Olson 1997). There have been no reports of increased adrenal disease in cat populations secondary to gonadectomy, and any impact on dog populations has not been reported.

Diabetes Mellitus in Cats

Cats have a 2- to 9-fold increased risk of developing of diabetes mellitus after neutering, with Burmese cats reported to be especially susceptible (Panciera et al. 1990; Rand et al. 1997; McCann et al. 2007; Prahl et al. 2007). One hypothesis is that this is because of decreased insulin sensitivity (Hoenig and Ferguson 2002; Kanchuk et al. 2002). Obesity also is associated with decreased insulin sensitivity and may be a confounding factor.

Hypothyroidism

Risk of hypothyroidism in dogs was reported to be increased with neutering in some studies (Milne and Hayes 1981; Panciera 1994) and not to be associated with neutering in other studies (Dixon and Mooney 1999a; Dixon et al. 1999b) Gonadectomy is associated with persistent increase in blood concentrations of gonadotropins (Lofstedt and VanLeeuwen 2002), many of which share molecular configuration with TSH in protein subunit chains and in glycosylation. It can be hypothesized that persistent high concentrations of gonadotropins lead to altered formation or glycosylation of TSH, and subsequent change in thyroid function. However, one study showed no change in resting serum TSH or thyroxin concentrations, or alterations in stimulus testing with thyroid releasing hormone when comparing castrated to intact male beagles (Gunzel-Apel et al. 2009).

Metabolic Disorders

Obesity

In retrospective studies, up to 2.8% of the canine population has been demonstrated to be obese, with up to 50% of gonadectomized dogs and cats designated as obese (Mason 1970; David and Rajendran 1980). Increase in indiscrimate appetite was reported in spayed bitches in one study but in another study of spayed and castrated dogs, no change in food intake or depth of back fat was reported by 15 months of age (O'Farrell and Peachey 1990; Salmeri et al. 1991a). Risk factors other than gonadectomy include housing of the animal; increasing age; ownership by an overweight person or a person over 40 years of age; and breed, with the beagle, cairn terrier, cavalier King Charles spaniel, cocker spaniel, dachshund and Labrador retriever among those breeds at greatest risk (Mason 1970; Edney and Smith 1986; Crane 1991; Sloth 1992; Colliard et al. 2006). In cats, castration and OHE are associated with increased risk of obesity, with one paper describing a 3.4-fold risk factor (Fettman et al. 1997; Kanchuk et al. 2002; Nguyen et al. 2004). Gonadectomized cats have increased body weight, increased body mass index, increased depth of the

falciform fat pad, decreased activity and decreased metabolic rate (Root 1995; Root et al. 1996; Stubbs et al. 1996; Fettman et al. 1997). Castrated cats also have an increase in serum concentrations of insulin growth factor I, prolactin and leptin, all of which are associated with metabolic rate and fat metabolism (Martin et al. 2006).

Lifespan

Most studies evaluating lifespan suggest that neutered animals live longer than intact animals (Kraft 1998; Greer et al. 2007). Increased lifespan in castrated male dogs may be due to a decrease in risky sexually dimorphic behaviours such as roaming, or to increased owner investment in the animal's care (Bronson 1982; Michell 1999; Moore et al. 2001). Castrated cats have reduced mortality compared with intact cats (Kalz 2001).

One study evaluating lifespan in a group of exceptionally long-lived rottweilers showed increased lifespan if left intact (Waters et al. 2009). This could be due to specific genetic factors in this population of dogs, to hormonal changes not yet identified, or to a lower incidence of obesity in this group; obesity itself has a negative effect on life expectancy (Greer et al. 2007).

It has been suggested that studies that separate dogs into intact or neutered categories at the time of disease onset or death create an artificial black-or-white evaluation of data regarding benefits and detriments of gonadectomy (Waters et al. 2011). Future studies that will guide this debate include those defining lifelong effects of exposure to gonadal hormones or better relating time of neuter to onset of disease.

Conflicts of interest

None of the authors have any conflicts of interest to declare.

References

- Alexander SA, Shane SM, 1994: Characteristics of animals adopted from an animal control center whose owners complied with a spaying/neutering program. J Am Vet Med Assoc 205, 472–476.
- Angioletti A, DeFrancesco I, Vergottini M, Battocchio ML, 2004: Urinary incontinence after spaying in the bitch: incidence and oestrogen therapy. Vet Res Commun **28**(Suppl 1), 153–155.
- Arnold S, 1997: Urinary incontinence in castrated bitches. Part I. Significance, clinical aspects and etiopathogenesis. Schweiz Arch Tierheilkd 139, 271–276.
- Aronsohn MG, Faggella AM, 1993: Surgical techniques for neutering 6 to 14-week-old kittens. J Amer Vet Med Assoc 202, 53–55.
- Atalan G, Holt PE, Barr FJ, 1998: Ultrasonographic assessment of bladder neck mobility in continent bitches and bitches with urinary incontinence attributable to urethral sphincter mechanism incompetence. Amer J Vet Res **59**, 673–679.
- Babon JE, Li X, Lei ZM, Sanfilippo JS, Yussman MA, Rao CV, 1996: Novel presence of luteinising hormone/chorionic gonadotropin receptors in human adrenal glands. J Clin Endocrinol Metab 81, 2397–2400.
- Bell FW, Klausner JS, Hayden DW, Feeney DA, Johnston SD, 1991: Clinical and pathologic features of prostatic adenocarcinoma in sexually intact and castrated dogs: 31 cases (1970–1987). J Amer Vet Med Assoc 199, 1623–1630.
- Berry SJ, Strandberg JD, Saunders WJ, Coffey DS, 1986: Development of canine benign prostatic hyperplasia with age. Prostate **9**, 363–373.
- Borchelt PL, 1983: Aggressive behavior of dogs kept as companion animals: classification and influence of sex, reproductive status and breed. Appl Anim Ethol 10, 45–61.
- Borchelt PL, Voith VL, 1987: Aggressive behavior in cats. Comp Cont Ed 9, 49–57.
- Brodbelt D, 2009: Perioperative mortality in small animal anaesthesia. Vet J **182**, 152–161

- Brodbelt DC, 2010: Feline anesthetic deaths in veterinary practice. Top Comp Anim Med 25, 189–194.
- Brodbelt DC, Pfeiffer DU, Young LE, Wood JL, 2008: Results of the confidential enquiry into perioperative small animal fatalities regarding risk factors for anesthetic-related death in dogs. J Amer-Vet Med Assoc 233, 1096–1104.
- Brodey RS, Goldschmidt MH, Roszel JR, 1983: Canine mammary gland neoplasms. J Amer Anim Hosp Assoc 19, 61–90.
- Bronson RT, 1982: Variation in age at death of dogs of different sexes and breeds. Amer J Vet Res **43**, 2057–2059.
- Burrow B, Batchelor D, Cripps P, 2005: Complications observed during and after ovariohysterectomy of 142 bitches at a veterinary teaching hospital. Vet Rec 157, 829–833.
- Caney SM, Holt PE, Day MJ, Rudorf H, Gruffydd-Jones TJ, 1998: Prostatic carcinoma in two cats. J Sm Anim Prac 39, 140–143.
- Carpenter J, Andrews L, Holsworth J, 1987: Tumors and tumor-like lesions. In: Holzworth J (ed), Diseases of the Cat. WB Saunders, Philadelphia PA, pp. 406–411.
- Chun R, DeLorimer L-P, 2003: Update on the biology and management of canine osteosarcoma, Vet Clin NA 33, 491–516.
- Colliard L, Ancel J, Benet JJ, Paragon BM, Blanchard G, 2006: Risk factors for obesity in dogs in France. J Nutr 136, 1951S–1954S.
- Cooley DM, Beranek BC, Schlittler DL, Glickman NW, Glickman LT, Waters DJ, 2002: Endogenous gonadal hormone exposure and bone sarcoma risk. Canc Epidemiol Biomark Prev 11, 1434–1440.
- Cotchin E, 1951: Neoplasms in small animals. Vet Rec **63**, 67–72.
- Crane SW, 1991: Occurrence and management of obesity in companion animals. J Sm Anim Prac 32, 275–282.
- David G, Rajendran EI, 1980: The after-effects of spaying in bitches and cats. Cheiron 9, 193–195.
- Dixon RM, Mooney CT, 1999a: Canine serum thyroglobulin autoantibodies in

- health, hypothyroidism and non-thyroidal illness. Res Vet Sci **66**, 243–246.
- Dixon RM, Reid SW, Mooney CT, 1999b: Epidemiological, clinical haematological and biochemical characteristics of canine hypothyroidism. Vet Rec **145**, 481–487.
- Donnay I, Rauis J, Devleeshouwer N, Wouters-Ballman P, Leclercq G, Verstegen J, 1995: Comparison of estrogen and progesterone receptor expression in normal and tumor mammary tissues from dogs. Amer J Vet Res **56**, 1188–1194.
- Dorn CR, Taylor DON, Frye FL, Hibbard HH, 1968a: Survey of animal neoplasms in Alameda and Contra Costa Counties, California. I. Methodology and description of cases. J Natl Canc Inst **40**, 295–205
- Dorn CR, Taylor DON, Schneider R,
 Hibbard HH, Klauber MR, 1968b: Survey of animal neoplasms in Alameda and Contra Costa Counties, California. II.
 Cancer morbidity in dogs and cats from Alameda County. J Natl Canc Inst 40, 307 318
- Duch DS, Chow FC, Hamar DW, Lewis LD, 1978: The effect of castration and body weight on the occurrence of the feline urological syndrome. Fel Prac 8, 35,40
- Duffy DL, Serpell JA, 2006: Non-reproductive effects of spaying and neutering on behavior in dogs. Proceedings, Symposium on non-surgical contraceptive methods for pet population control, Alexandra VA
- Duval JM, Budsberg SC, Flo GL, Sammarco JL, 1999: Breed, sex, and body weight as risk factors for rupture of the cranial cruciate ligament in young dogs. J Amer Vet Med Assoc 215, 811–814.
- Edney ATB, Smith PM, 1986: Study of obesity in dogs visiting veterinary practices in the United Kingdom. Vet Rec 118, 391–396.
- Eze CA, Eze MC, 2002: Castration, other management practices and socio-economic implications for dog keepers in Nsukka area, Enugu State, Nigeria. Prev Vet Med 55, 273–280.

- Faggella AM, Aronsohn MG, 1993: Anesthetic techniques for neutering 6- to 14-week-old kittens. J Amer Vet Med Assoc 202. 56–62.
- Faggella AM, Aronsohn MG, 1994: Evaluation of anesthetic protocols for neutering 6–14-week old pups. J Amer Vet Med Assoc 205, 308–314.
- Fettman MJ, Stanton CA, Banks LL, Hamar DW, Johnson DE, Hegstad RL, Johnston S, 1997: Effects of neutering on bodyweight, metabolic rate and glucose tolerance of domestic cats. Res Vet Sci **62**, 131–136.
- Fidler IJ, Brodey RS, 1967: The biological behavior of canine mammary neoplasms. J Amer Vet Med Assoc **151**, 1311–1318.
- Foster SJ, 1967: The 'urolithiasis' syndrome in male cats: a statistical analysis of the problems, with clinical observations. J Sm Anim Prac 8, 207–214.
- Greenfield CL, Johnson SL, Schaeffer DJ, 2004: 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 Amer Vet Med Assoc 224, 1780–1787.
- Greer KA, Canterberry SC, Murphy KE, 2007: Statistical analysis regarding the effects of height and weight on life span of the domestic dog. Res Vet Sci 82, 208– 214
- Gregory SP, Parkinson TJ, Holt PE, 1992: Urethral conformation and position in relation to urinary incontinence in the bitch. Vet Rec 131, 167–170.
- Gregory SP, Holt PE, Parkinson TJ, Wathes CM, 1999: Vaginal position and length in the bitch: relationship to spaying urinary incontinence. J Sm Anim Prac **40**, 180–184.
- Gunzel-Apel AR, 1998: Early castration of dogs and cats from the point of view of animal welfare. Dtsch Tierarztl Wochenschr 105, 95–98.
- Gunzel-Apel AR, Seefeldt A, Eschricht FM, Urhausen C, Kramer S, Mischke R, Hoppen HO, Beyerbach M, Koivisto M, Dieleman SJ, 2009: Effects of gonadectomy on prolactin and LH secretion and the pituitary-thyroid axis in male dogs. Theriogenology 71, 746–753.
- Hagman R, Lagerstedt AS, Hedhammer A, Egenvall A, 2011: A breed-matched case-control study of potential risk-factors for canine pyometra. Theriogenology 75, 1251–1257.
- Hahn KA, VonDerHaar MA, Teclaw RF, 1992: An epidemiological evaluation of 1202 dogs with testicular neoplasia [Abstract]. J Vet Intern Med 6, 121.
- Hamilton JM, Else RW, Forshaw P, 1977: Oestrogen receptors in canine mammary tumours. Vet Rec 101, 258–260.
- Hampe JF, Misdorp W, 1974: Tumours and dysplasias of the mammary gland. Bull World Health Org 50, 111–133.
- Harasen G, 2003: Canine cranial cruciate ligament rupture in profile. CanVet J 44, 845–846.
- Hart BL, 1973: Behavioral effects of castration. Fel Prac 3, 10–12.
- Hart BL, 1979: Problems with objectionable sociosexual behavior of dogs and cats:

- therapeutic use of castration and progestins. Comp Cont Ed 1, 461–465.
- Hart BL, 2001: Effect of gonadectomy on subsequent development of age-related cognitive impairment in dogs. J Amer Vet Med Assoc 219, 51–56.
- Hart BL, Barrett RE, 1973: Effects of castration on righting, roaming, and urine spraying in adult male cats. J Amer Vet Med Assoc 163, 290–292.
- Hart BL, Eckstein RA, 1997: The role of gonadal hormones in the occurrence of objectionable behaviours in dogs and cats. Appl Anim Behav Sci 52, 331–344.
- Hawe RS, 1983: What is your diagnosis? Prostatic adenocarcinoma. J Amer Vet Med Assoc 182, 1257–1258.
- Hayes HM, Milne KL, Mandel CP, 1981: Epidemiological features of feline mammary carcinoma. Vet Rec 108, 476–479.
- Herron MA, 1972: The effect of prepubertal castration on the penile urethra of the cat. J Amer Vet Med Assoc **160**, 208–211.
- Hoenig M, Ferguson DC, 2002: Effects of neutering on hormonal concentrations and energy requirements in male and female cats. Amer J Vet Res 63, 634–649.
- Holt PE, 2004: Urinary incontinence in the male and female dog or does sex matter? http://www.vin.com (accessed 1 October 2004)
- Holt PE, Thursfield MV, 1993: Association in bitches between breed, size, neutering and docking, and acquired urinary incontinence due to incompetence of the urethral sphincter mechanism. Vet Rec 133, 177–180.
- Hopkins SG, Schubert TA, Hart BL, 1976: Castration of adult male dogs: effects on roaming, aggression, urine marking, and mounting. J Amer Vet Med Assoc 168, 1108–1110.
- Houlton JEF, McGlennon NJ, 1992: Castration and physeal closure in the cat. Vet Rec 131, 466–467.
- Howe LM, 1997: Short-term results and complications of prerpubertal gonadectomy in cats and dogs. J Amer Vet Med Assoc 211, 57–62
- Howe LM, Slater MR, Boothe HW, Hobson HP, Fossum TW, Spann AC, Wilkie WS, 2000: Long-term outcome of gonadectomy performed at an early age or traditional age in cats. J Amer Vet Med Assoc 217, 1661–1665.
- Howe LM, Slater MR, Boothe HW, Hobson HP, Holcom JL, Spann AC, 2001: Long-term outcome of gonadectomy performed at an early age or traditional age in dogs. J Amer Vet Med Assoc 218, 217–221.
- Hubbard BS, Vulgamott LC, Liska WD, 1990: Prostatic adenocarcinoma in a cat. J Amer Vet Med Assoc 197, 1493–1494.
- Janowsky JS, 2006: The role of androgens in cognition and brain aging in men. Neuroscience **138**, 1015–1020.
- Johnson RT, Burk JA, 2006: Effects of gonadectomy and androgen supplementation on attention in male rats. Neurobiol Learn Memory 85, 219–227.
- Johnson-Delaney CA, 2006: Ferret adrenal disease: 2006 perspective. Exotic DVM 8,
- Johnston SD, Root Kustritz MV, Olson PN, 2001a: Disorders of the canine uterus and

- uterine tubes (oviducts). In Johnston SD, Root Kustritz MV, Olson PN (eds), Canine and Feline Theriogenology. WB Saunders, Philadelphia PA, pp. 206–224.
- Johnston SD, Root Kustritz MV, Olson PN, 2001b: Disorders of the feline uterus and uterine tubes (oviducts). In Johnston SD, Root Kustritz MV, Olson PN (eds), Canine and Feline Theriogenology. WB Saunders, Philadelphia PA, pp. 463–471.
- Kalz B, 2001: Population biology, space use and behavior of feral cats and measures to control reproduction. Inaugural dissertation, Mathematics and Science Faculty, Humboldt University, Berlin [German].
- Kanchuk ML, Backus RC, Calvert CC, Morris JG, Rogers QR, 2002: Neutering induces changes in food intake, body weight, plasma insulin and leptin concentrations in normal and lipoprotein lipase-deficient male cats. J Nutr 132, 1730–1732.
- Knapp DW, Glickman NW, DeNicola DB, Bonney PL, Lin TL, Glickman LT, 2000: Naturally-occurring canine transitional cell carcinoma of the urinary bladder. A relevant model of human invasive bladder cancer. Urol Oncol 5, 47–59.
- Kraft W, 1998: Geriatrics in canine and feline internal medicine. Eur J Med Res 3, 31–41.
- Kritzer MF, Brewer A, Montalmant F, Davenport M, Robinson JK, 2007: Effects of gonadectomy on performance in operant tasks measuring prefrontal cortical function in adult male rats. Horm Beh 51, 183–194.
- Lawrence HJ, Gould WJ, Flanders JA, Rowland PH, Yaeger AE, 1993: Unilateral adrenalectomy as a treatment for adrenocortical tumors in ferrets: five cases (1990–1992). J Amer Vet Med Assoc 203, 267–270.
- LeRoy BE, Lech ME, 2004: Prostatic carcinoma causing urethral obstruction and obstipation in a cat. J Fel Med Surg 6, 397–400.
- Lofstedt RM, VanLeeuwen JA, 2002: Evaluation of a commercially available luteinizing hormone test for its ability to distinguish between ovariectomized and sexually intact bitches. J Amer Vet Med Assoc 220, 1331–1335.
- Lowseth LA, Gerlach RF, Gillett NA, Muggenburg BA, 1990: Age-related changes in the prostate and testes of the beagle dog. Vet Path 27, 347–353.
- Mahlow JC, 1999: Estimation of the proportions of dogs and cats that are surgically sterilized. J Amer Vet Med Assoc **215**, 640–643.
- Manning AM, Rowan AN, 1992: Companion animal demographics and sterilization status: results from a survey in four Massachusetts towns. Anthrozoos 5, 192–201.
- Martin LJM, Siliart B, Dumon HJW, Nguyen P, 2006: Spontaneous hormonal variations in male cats following gonadectomy. J Fel Med Surg **8**, 309–314.
- Mason E, 1970: Obesity in pet dogs. Vet Rec **86**, 612–616.
- May C, Bennett D, Downham DY, 1991: Delayed physeal closure with castration in cats. J Sm Anim Prac **32**, 326–328.

- McCann TM, Simpson KE, Shaw DJ, Butt JA, Gunn-Moore DA, 2007: Feline diabetes mellitus in the UK: the prevalence within an insured cat population and a questionnaire-based putative risk factor analysis. J Fel Med Surg **9**, 289–299.
- McNicholas WT, Wilkens BE, Blevins WE, Snyder PW, McCabe GP, Applewhite AA, Laverty PH, Breur GJ, 2002: Spontaneous femoral capital physeal fractures in adults cats: 26 cases (1996– 2001). J Amer Vet Med Assoc 221, 1731– 1736.
- Michell AR, 1999: Longevity of British breeds of dogs and its relationship with sex, size, cardiovascular variables and disease. Vet Rec 145, 625–629.
- Miller DM, 1995: Ovarian remnant syndrome in dogs and cats: 46 cases (1988–1992). J Vet Diagn Invest 7, 572–574.
- Milne KL, Hayes HM, 1981: Épidemiologic features of canine hypothyroidism. Cornell Vet 71, 3–14.
- Misdorp W, Hart AAM, 1979: Canine mammary cancer. II. Therapy and causes of death. J Sm Anim Prac 20, 395–404.
- Moe L, 2001: Population-based incidence of mammary tumors in some dogs breeds. J Reprod Fert Suppl 57, 439–443.
- Mondelli F, Previde EP, Verga M, Levi D, Magistrelli S, Valsecchi P, 2004: The bond that never developed: adoption and relinquishment of dogs in a rescue shelter. J Appl Anim Welf Sci 7, 253–266.
- Mong JA, Pfaff DW, 2003: Hormonal and genetic influences underlying arousal as it drives sex and aggression in animal and human brains. Neurobiol Aging **24**, 583–588
- Moore GE, Burkman KD, Carter MN, Peterson MR, 2001: Causes of death or reasons for euthanasia in military working dogs: 927 cases (1993–1996). J Am Vet Med Assoc **219**, 209–214.
- Moulton JE, Taylor DON, Dorn CR, Andersen AC, 1970: Canine mammary tumors. Path Vet **7**, 289–320.
- Nassar R, Talboy J, Moulton C, 1992: Animal Shelter Reporting Study 1990. American Humane Association, Englewood CO.
- National Council on Pet Population Study and Policy, 1994: National Shelter Census: 1994 Results. NCCPPSP, Fort Collins CO.
- Neilson JC, Eckstein RA, Hart BL, 1997: Effects of castration on problem behaviors in male dogs with reference to age and duration of behavior. J Amer Vet Med Assoc 211, 180–182.
- New JG, Salman MD, King M, Scarlett JM, Kass PH, Hutchison JM, 2000: Shelter relinquishment: characteristics of shelterrelinquished animals their owners compared with animals and their owners in US pet-owning households. J Appl Anim Welf Sci 3, 179–201.
- New JC, Kelch WJ, Hutchison JM, Salman MD, King M, Scarlett JM, Kass PH, 2004: Birth and death rate estimates of cats and dogs in U.S. households and related factors. J Appl Anim Welf Sci 7, 229–241.
- Nguyen PG, Dumon HJ, Siliart BS, Martin LJ, Sergheraert R, Biourge VC, 2004: Effects of dietary fat and energy on body

- weight and composition after gonadectomy in cats. Amer J Vet Res **65**, 1708–1713.
- Norris AM, Laing EJ, Valli VE, Withrow SJ, Macy DW, Ogilvie GK, Tomlinson J, McCaw D, Pidgeon G, Jacobs RM, 1992: Canine bladder and urethral tumors: a retrospective study of 115 cases (1980-1985). J Vet Intern Med **6**, 145–153.
- Obradovich J, Walshaw R, Goulland E, 1987: The influence of castration on the development of prostatic carcinoma in the dog: 43 cases (1978–1985). J Vet Intern Med 1, 183–187.
- O'Farrell V, Peachey E, 1990: Behavioural effects of ovariohysterectomy on bitches. J Sm Anim Prac 31, 595–598.
- Olson PN, 1997: Early spay and neuter. Proceedings, North American Veterinary Conference, Orlando FL.
- Panciera DL, 1994: Hypothyroidism in dogs: 66 cases (1987–1992). J Amer Vet Med Assoc **204**, 761–767.
- Panciera DL, Thomas CB, Eicker SW, Atkins CE, 1990: Epizootiologic patterns of diabetes mellitus in cats: 333 cases (1980–1986). J Amer Vet Med Assoc 197, 1504–1508.
- Patronek GJ, Glickman LT, Beck AM, McCabe GC, Ecker C, 1996a: Risk factors for relinquishment of dogs to an animal shelter. J Amer Vet Med Assoc 209, 572–581.
- Patronek GJ, Glickman LT, Beck AM, McCabe GC, Ecker C, 1996b: Risk factors for relinquishment of cats to an animal shelter. J Amer Vet Med Assoc 209, 582–588.
- PetSmart Charities A&U Barriers, 2002: http://www.petsmartcharities.org/resources/ resources-documents/PetSmartCharities_ Research_AUBarriers.pdf (accessed 19 December 2011).
- Poirier VJ, Forrest JL, Adams WM, Vail DM, 2004: Piroxicam, mitoxantrone, and coarse fraction radiotherapy for the treatment of transitional cell carcinoma of the bladder in 10 dogs: a pilot study. J Amer Anim Hosp Assoc 40, 131–136.
- Pollari FL, Bonnett BN, Bamsey SC, Meek AH, Allen DG, 1996: Postoperative complications of elective surgeries in dogs and cats determined by examining electronic and paper medical records. J Amer Vet Med Assoc 208, 1882–1886.
- Ponglowhapan S, Church DB, Khalid M, 2008a: Differences in the expression of luteinizing hormone and follicle-stimulating hormone receptors in the lower urinary tract between intact and gonadectomised male and female dogs. Dom Anim Endo 34, 339–351.
- Ponglowhapan S, Church DB, Khalid M, 2008b: Differences in the proportion of collagen and muscle in the canine lower urinary tract with regard to gonadal status and gender. Theriogenology **70**, 1516–1524.
- Ponglowhapan S, Church DB, Khalid M, 2011: Effect of the gonadal status and the gender on glycosaminoglycans profile in the lower urinary tract of dogs. Theriogenology **76**, 1284–1292.
- Potter K, Hancock DH, Gallina AM, 1991: Clinical and pathologic features of endometrial hyperplasia, pyometra, and endo-

- metritis in cats: 79 cases (1980–1985). J Amer Vet Med Assoc 198, 1427–1431.
- Prahl A, Guptill L, Glickman NW, Tetrick M, Glickman LT, 2007: Time trends and risk factors for diabetes mellitus in cats presented to veterinary teaching hospitals. J Fel Med Surg 9, 351–358.
- Priester WA, McKay FW, 1980: The occurrence of tumors in domestic animals. Natl Canc Inst Monogr **54**, 169.
- Priester WA, Mulvihill JJ, 1972: Canine hip dysplasia: relative risk by sex, size, and breed, and comparative aspects. J Amer Vet Med Assoc 160, 735–739.
- Prymak C, McKee LJ, Goldschmidt MH, Glickman LT, 1988: Epidemiologic, clinical, pathologic, and prognostic characteristics of splenic hemangiosarcoma and splenic hematoma in dogs: 217 cases (1985). J Amer Vet Med Assoc 193, 706–712
- Ragetly CA, Evans R, Mostafa AA, Griffon DJ, 2011: Multivariate analysis of morphometric characteristics to evaluate risk factors for cranial cruciate ligament deficiency in Labrador retrievers. Vet Surg 40, 327–333.
- Rand JS, Bobbermien LM, Hendrikz JK, Copland M, 1997: Over representation of Burmese cats with diabetes mellitus. Aust Vet J **75**, 402–405.
- Reichler IM, 2009: Gonadectomy in cats and dogs: a review of risks and benefits. Reprod Dom Anim 44(Suppl 2), 29–35.
- Reisner IR, Houpt KA, Shofer FS, 2005: National survey of owner-directed aggression in English Springer Spaniels. J Amer Vet Med Assoc 227, 1594–1603.
- Richards HG, McNeil PE, Thompson H, Reid SWJ, 2001: An epidemiological analysis of canine-biopsies database compiled by a diagnostic histopathology service. Prev Vet Med **51**, 125–136.
- Romagnoli S, 2008: Surgical gonadectomy in the bitch and queen: should it be done and at what age? Proceedings, Southern European Veterinary Conference and Congreso Nacional AVEPA, Barcelona Spain.
- Root MV, 1995: Early spay-neuter in the cat: effect on development of obesity and metabolic rate. Vet Clin Nutr **2**, 132–134.
- Root Kustritz MV, 1996: Elective gonadectomy in the cat. Fel Prac **24**, 36–39. Root Kustritz MV, 1999: Early spay-neuter
- Root Kustritz MV, 1999: Early spay-neuter in the dog and cat. Vet Clin NA **29**, 935–943.
- Root Kustritz MV, 2005: Reproductive behavior of small animals. Theriogenology **64**, 743–746.
- Root Kustritz MV, 2007: Determining the optimal age for gonadectomy of dogs and cats. J Amer Vet Med Assoc **231**, 1665–1675.
- Root Kustritz MV, 2010: Optimal age for gonadectomy in dogs and cats. Clin Therio **2**, 177–181.
- Root MV, Johnston SD, Johnston GR, Olson PN, 1996a: The effect of prepuberal and postpuberal gonadectomy on penile extrusion and urethral diameter in the domestic cat. Vet Radiol Ultrasound 37, 363–366.
- Root MV, Johnston SD, Olson PN, 1996b: Effect of prepuberal and postpuberal gonadectomy on heat production mea-

sured by indirect calorimetry in male and female domestic cats. Amer J Vet Res **57**, 371–374

- Root MV, Johnston SD, Olson PN, 1996c: The effect of prepuberal and postpuberal gonadectomy on radial physeal closure in male and female domestic cats. Vet Radiol Ultrasound 38, 42–47.
- Rosenthal KL, Peterson ME, Quesenberry KE, Hillyer EV, Beeber NL, Moroff SD, Lothrop CD, 1993: Hyperadrenocorticism associated with adrenocortical tumor or nodular hyperplasia of the adrenal gland in ferrets: 50 cases (1987–1991). J Amer Vet Med Assoc 203, 271–275.
- Ru G, Terracini B, Glickman LT, 1998: Host related risk factors for canine osteosarcoma. Vet J 156, 31–39.
- Salmeri KR, Bloomberg MS, Scruggs SL, Shille V, 1991a: Gonadectomy in immature dogs: effects of skeletal, physical, and behavioral development. J Amer Vet Med Assoc 198, 1193–1203.
- Salmeri KR, Olson PN, Bloomberg MS, 1991b: Elective gonadectomy in dogs: a review. J Amer Vet Med Assoc 198, 1183– 1192
- Schneider R, Dorn CR, Taylor DON, 1969: Factors influencing canine mammary cancer development and postsurgical survival. J Natl Canc Inst 43, 1249–1261.
- Schoemaker NJ, Teerds KJ, Mol JA, 2002: The role of luteinizing hormone in the pathogenesis of hyperadrenocorticism in neutered ferrets. Mol Cell Endocrinol 197, 117–125
- Slauterbeck JR, Pankratz K, Xu KT, Bozeman SC, Hardy DM, 2004: Canine ovariohysterectomy and orchiectomy increases the prevalence of ACL injury. Clin Orthop 429, 301–305.
- Sloth C, 1992: Practical management of obesity in dogs and cats. J Sm Anim Prac 33, 178–182.
- Smith AN, 2003: Hemangiosarcoma in dogs and cats. Vet Clin NA 33, 533–552.

Sorenmo K, 2003: Canine mammary gland tumors. Vet Clin NA **33**, 573–596.

- Sorenmo KU, Goldschmidt M, Shofer F, Goldkamp C, Ferracone J, 2003: Immunohistochemical characterization of canine prostatic carcinoma and correlation with castration status and castration time. Vet Comp Oncol 1, 48–56.
- Spain CV, Scarlett JM, Houpt KA, 2004a: Long-term risks and benefits of early-age gonadectomy in cats. J Amer Vet Med Assoc 224, 372–379.
- Spain CV, Scarlett JM, Houpt KA, 2004b: Long-term risks and benefits of early-age gonadectomy in dogs. J Amer Vet Med Assoc 224, 380–387.
- Stocklin-Gautschi NM, Hassig M, Reichler IM, 2001: The relationship of urinary incontinence to early spaying in bitches. J Reprod Fertil **57**, 233–236.
- Stubbs WP, Bloomberg MS, Scruggs SL, Shille VM, Lane TJ, 1996: Effects of prepubertal gonadectomy on physical and behavioral development in cats. J Amer Vet Med Assoc **209**, 1864–1871.
- Teske E, Naan EC, VanDijk EM, VanGarderen E, Schalken JA, 2002: Canine prostate carcinoma: epidemiological evidence of an increased risk in castrated dogs. Mol Cell Endocrinol 197, 251–255.
- Trevejo R, Yang M, Lund EM, 2011: Epidemiology of surgical castration in dogs and cats in the United States. J Amer Vet Med Assoc 238, 898–904.
- VanHagen MA, Ducro BJ, VanDenBroek J, Knol BW, 2005: Incidence, risk factors, and heritability estimates of hind limb lameness caused by hip dysplasia in a birth cohort of boxers. Amer J Vet Res 66, 307–312.
- Verstegen J, Onclin K, 2003a: Mammary tumors in the queen. Proceedings, Society for Theriogenology Annual Meeting, Columbus OH.
- Verstegen J, Onclin K, 2003b: Etiopathogenesis, classification and prognosis of mammary tumors in the canine and feline

- species. Proceedings, Society for Theriogenology Annual Meeting, Columbus OH.
- Ware WA, Hopper DL, 1999: Cardiac tumors in dogs: 1982-1995. J Vet Intern Med 13, 95–103.
- Waters DJ, Shen S, Glickman LT, 2000: Life expectancy, antagonistic pleiotropy, and the testis of dogs and men. Prostate **43**, 272–277.
- Waters DJ, Kengeri SS, Clever B, Booth JA, Maras AH, Schlittler DL, Hayek MG, 2009: Exploring mechanisms of sex differences in longevity: lifetime ovary exposure and exceptional longevity in dogs. Aging Cell 8, 752–755.
- Waters DJ, Kengeri SS, Maras AH, Chiang EC, 2011: Probing the perils of dichotomous binning: how categorizing female dogs as spayed or intact can misinform our assumptions about the lifelong health consequences of ovariohysterectomy. Theriogenology **76**, 1496–1500.
- White CR, Hohenhaus AE, Kelsey J, Procter-Gray E, 2006: Cutaneous MCTs: associations with spay/neuter status, breed, body size, and phylogenetic cluster. J Amer Anim Hosp Assoc 47, 210–216.
- Whitehair JG, Vasseur PB, Willits NH, 1993: Epidemiology of cranial cruciate ligament rupture in dogs. J Amer Vet Med Assoc **203**, 1016–1019.
- Wright JC, Nesselrote MS, 1987: Classification of behavior problems in dogs: distributions of age, breed, sex and reproductive status. Appl Anim Beh Sci 19, 169–178.
- Zirkin BR, Strandberg JD, 1984: Quantitative changes in the morphology of the aging canine prostate. Anat Rec 208, 207–214.

Author's address (for correspondence): Dr MV Root Kustritz, University of Minnesota College of Veterinary Medicine, 1352 Boyd Avenue, St. Paul, MN 55108, USA. E-mail: rootk001@umn.edu