Wilsonville Veterinary Clinic
Phone: (503) 682-3737
Fax: (503) 682-3540

REPRODUCTIVE REVOLUTIONS
Phone: (503) 982-5701
Fax: (503) 982-5718

Benefits and Risks of the Gonadal Steroids: A Review

There is new research being published daily on the benefits and risks of exposure to the gonadal steroids. When considering if and when to neuter your pet, the more information available, the more informed a decision the client is able to make. This paper will discuss the benefits and risks of the gonadal steroids by categorizing them as follows: cancer; orthopedic diseases; behavior; medical conditions; longevity or lifespan; contraception; anesthestic and surgical complications[1–17]. In this paper, the terms gonadectomy, neuter, spay or variations thereof will indicate an animal that has had its testicles or ovaries removed; while the term intact will indicate animals who still have their testicles or ovaries in place.

Cancer

Numerous factors affect the risk and prevalence of different types of cancer in companion animals including genetics; breed, age, viral infection, environment, chronic inflammation and gonadal status.

Mammary gland: Mammary gland tumors are the most common tumor in female dogs. Approximately 50% of mammary tumors are benign and 50% are malignant. In the US, the incidence of mammary cancer is much lower than in other countries where animals have traditionally been spayed at young ages compared to other countries where spaying is uncommon. Age, hormonal exposure and breed are the 3 biggest contributing factors to the incidence of mammary cancer. Intact females are 3-7x more likely to develop mammary cancer than spayed females. There is a protective effect of spaying prior to the first heat with these bitches having an incidence of 0.05%; those spayed between their first and second heat having an incidence of 8%; and those spayed after their second heat having an incidence of 26%.

Genitourinary tumors: Ovarian tumors occurly uncommonly (0.5-1.4% of tumors reported). Malignancy occurs in approximately 50% of cases. Uterine tumors are uncommon (0.3-0.4% of tumors reported). Benign tumors are more common than malignant ones. Vaginal and vulvar tumors are slightly more common, accounting for 2.4 – 3% of all tumors reported and may be hormonally dependent since they tend to occur in intact females. Transmissible venereal tumors are most common in free roaming males and females in tropical climates. They are malignant in 5-17% of the cases. Testicular tumors occur commonly, accounting for 16-27% of tumors in intact male dogs and 90% of all tumors of the male reproductive tract. Most testicular tumors are benign although some are hormonally active. Testicular tumors are much more common in cryptorchid

testicles, so all cryptorchid males should have the retained testicle(s) removed by 2 years of age to reduce risk of tumor formation. Prostatic cancer is rare and occurs 3.6-4.34 times more likely in neutered males and has an overall incidence of 0.29- 0.6% of all reported tumors. It is almost always malignant and aggressive in its behavior. Tumors of the bladder and urethra are uncommon, accounting for 2% of all tumors reported. Spaying and neutering increase the risk of developing malignant transitional cell tumors 2.03 times compared to intact animals.

Lymphoma: This is a tumor of the white blood cells or lympatic organs is one of the most commonly diagnosed cancers in dogs. Remission occurs in 60-90% of treated animals for at least some period of time, although cure is rare. In one study, intact male, spayed female and neutered male dogs were more likely to develop lymphoma than intact female dogs. In Viszlas, lymphoma was more likely in neutered males or females. In studies with Labrador Retrievers and German Shepherd dogs (GSD) there was no clear associations between gonadal status and incidence of lymphoma. In Golden Retrievers, spaying or neutering after 1 year of age was associated with decreased risk of lymphoma.

Mast cell tumors: This skin tumor accounts for 16-21% of all skin tumors in dogs. Spayed females appear to be at 4.11x greater risk for development of these tumors compared to intact females. Spayed Viszlas were 3.5x more likely to develop MCT than intact bitches. There was no difference in MCT risk in Labrador Retrievers, Golden Retrievers or GSD.

Hemangiosarcoma: These tumors of the blood organs (liver, spleen and heart) represent 5-7% of all non-skin malignant tumors in dogs. It is an aggressive tumor with a poor prognosis because metastasis is common prior to diagnosis. Spayed females were 2.2x more likely to develop hemangiosarcoma than intact females of various breeds. There was no overall effect of neuter status in male Golden Retrievers or Viszlas on tumor incidence however, there was an increased incidence of hemangiosarcoma in male and female Viszlas and female Golden Retreivers that were spayed or neutered after to 1 year of age. There was also increased risk of hemangiosarcoma in spayed female Viszlas regardless of whether they were spayed prior to or after 1 year of age. There appears to be no change in incidence in hemangiosarcoma in GSD regardless of sex or age at neutering. There is a 1.6 and 4.38x increased risk of cardiac hemangiosarcoma in spayed and neutered animals respectively, of various breeds, although the incidence of this particular type of hemangiosarcoma is very low (0.19% of all tumors reported).

Osteosarcoma: This is the most common primary bone tumor in dogs. It is very aggressive and holds a poor prognosis for survival for more than 1 year after diagnosis. Large and giant breed dogs are at greatest risk for this type of cancer. Gonadectomized dogs of both sexes are 2x more likely than their intact counterparts. Both male and female Rottweilers, spayed or neutered before 1 year of age, had a 25% chance of developing osteosarcoma in their lifetimes. There may be benefit to the length of time there is exposure to gonadal steroids in terms of risk of developing osteosarcoma, in that animals that were sexually intact for less time, were at greater risk for osteosarcoma development; however, the age at which this benefit occurs has yet to be elucidated.

There was no difference in osteosarcoma risk in GSD regardless of neuter status or age at neutering.

Orthopedic disease

Cranial cruciate rupture (CCR) has an incidence of 1.7% in the overall population but is more common in large and giant breeds and in more young, active dogs. Factors implicated in CCR include differences in athletic ability, conformation, physical fitness and body condition as well as nutritional, genetic, degenerative disease, trauma, immune mediated arthritis and hormonal causes. One study showed a 3.8% increase in CCR in gonadectomized animals with the highest incidence in spayed females and this has been supported in other studies. It has been shown in Labrador Retrievers and Golden Retrievers that spaying and neutering increased the incidence of orthopedic joint diseases 2x and 3-5x respectively. GSD gonadectomized before 12 months of age were at increased risk for CCR.

Hip dysplasia has a incidence of 1.8% in the overall population but is more common in large and giant breed dogs. Its root causes are multifactorial - including genetic, environmental, nutritional, hormonal and likely other yet undetermined factors. Labrador Retrievers and Golden Retrievers are at increased risk for orthopedic joint diseases 2x and 3-5x respectively when they are gonadectomized. There was no increase in incidence of hip or elbow dysplasia in GSD neutered before 1 year of age. Elbow dysplasia was more common in male Labrador Retreivers neutered prior to 6 months of age compared to intact animals (2% vs 0.57%). Boxers neutered more than 6 months prior to a diagnosis of hip dysplasia were 1.5x more likely to develop hip dysplasia than intact animals (mean age for gonadectomy being 3 years of age). Pre-pubertal gonadectomy has been shown to result in an increased incidence of hip dysplasia (amongst similarly aged counterparts neutered after 5.5 months of age, but not compared to similarly aged intact animals) but the disease was not so severe in the study population to require surgical intervention or euthanasia, so the impact on health or longevity cannot be determined at this time.

Pre-pubertal gonadectomy is associated with increased bone length due to delayed closure of the growth plates and this has been speculated, but not yet proven, to be associated with increased risk of orthopedic disease later in life.

Behavior:

Gonadectomy reduces the negative behaviors associated with the gonadal hormones of roaming, aggressive behavior and urine marking. The age at which the surgery occurs does not appear to have any impact on the decrease in the behavior, at least in male dogs. While gonadectomy decreases intermale aggression, it may actually increase interfemale aggression. In GSD, spaying between 5-10 months of age increased their reactivity to unfamiliar dogs and people. Female dogs that display signs of aggressive behavior prior to gonadectomy are at highest risk for increased signs of this behavior post-gonadectomy, while there is little risk of this behavior developing if there are no signs of aggression prior to gonadectomy.

There is mixed data regarding behaviors such as activity level, excitability, submissive urination, and noise phobias. It appears that most of these difference may have something to do with age at gonadectomy and behavior prior to surgery. Animals spayed or neutered after 2 years of age appear to have little change in behavior and no increase in negative behaviors. In some studies, it has been showed that neutering prior to 5.5 months of age may have a negative impact on behaviors associated with confidence (submissive urination, noise phobia, excessive barking, aggression towards visitors or certain family members). Viszlas gonadectomized prior to 6 months of age were more likely to show signs of fear and anxiety compared to those gonadectomized later in life.

While there may be real concerns regarding the age at gonadectomy, more research is required in this area because of the many compounding factors associated with the reason animals were spayed or neutered and there are large differences in study design and animal populations. At this time, it is not possible to make definitive conclusions about the benefits or risks of gonadectomy at differing ages.

Other medical conditions:

Prostate diseases, including benign prostatic hyperplasia (BPH), prostatitis (chronic or acute) and prostatic cysts only predominantly in intact male dogs (93.3% of cases). By 5 years of age, 50% of intact male dogs are affected by BPH and by 9 years of age, 95-100% are affected. The presence of BPH predisposes to the development of prostatitis. Clinical signs may be apparent early in the course of the disease or may be subclinical for many years before they are noted.

Ovariohysterecomy prevents or treats disease of the uterus (pyometra, endometritis, metritis) and the ovaries (ovarian cysts or tumors), as well as preventing pregnancy and the medical conditions associated with it (difficult birth, gestational diabetes, metritis). The incidence of pyometra (pus in the uterus) is 23-24% in countries where ovariohysterectomy or ovariectomy is not commonly practiced as a means of population control. Ovarian tumors may predispose to pyometra due to hormone production by the tumor. Pyometra is an expensive condition to treat medically and has a very high recurrence rate (10-77%) and is associated with serious, life-threatening consequences like kidney failure and overwhelming bacterial infection (sepsis).

Urinary incontinence may result from ovariohysterectomy in between 2-20% of the population. It is more common in large and giant breeds. Females spayed before 3 months of age are at greatest risk; while spaying after the first heat does not change the risk. The age at gonadectomy may also affect the age when incontinence develops, with bitches spayed earlier in life developing signs at an earlier age. In GSD, spaying between 6-11 months may increase the risk of developing incontinence compared to sexually intact animals, but this conclusion needs further elucidation before applying it to recommendations on age at which to spay.

Obesity has been associated with gonadectomy, with body condition increasing in both males and females after surgery. Increased appetite and decreased metabolic rate are contributing factors. Increases in weight gain in the 2 – 24 months after surgery seem to

be the most significant so monitoring activity level and weight during this time frame may be the best way to prevent excessive weight gain. While gonadectomy may have a role in obesity, it is clearly a multifactorial problem and client education on diet and exercise along with careful weight monitoring in the 2 years after surgery will help maintain proper body condition regardless of neuter status.

At this time, there has been no proven correlation between hypothyroidism, adrenal disease and gonadectomy or sexually intact status. There has been no proven effect on trainability associated with neuter or intact status. Cognitive dysfunction has also been studied and to date there is no sufficient evidence one way or another to determine if there is an impact on cognitive dysfunction. There may be some association of gonadectomy and patellar luxation with gonadectomized dogs having a higher incidence of patellar luxation. However, this study did not evaluate age at gonadectomy, and factors such as body weight and age may factor into the disease, so further research is needed before accurate conclustions can be drawn.

Longevity and lifespan:
Gonadectomy, in general, is associated with increased lifespan (spayed females life expectancy increased by 26.3%; castrated males increased by 13.8%). While there may be increased risk of some tumors and immune mediated disease, there is decreased risk of infectious disease and trauma. In Rottweilers, bitches spayed after 4 years of age were more likely to reach 13 years of age than those spayed before that time; the trade of being that gonadectomized animals are at increased risk for osteosarcoma. In Viszlas, gonadectomized animals also have greater longevity than their sexually intact counterparts, but the gonadectomized animals were similar to the Rottweiler study, at increased risk for neoplasia.

Contraception:
It has been estimated that over half of the pregnancies that occur annually are unplanned. Gonadectomy is an effective means of controlling unwanted pregnancy. It is estimated that overpopulation results in relinquishment and euthanasia of millions of animals annually in the United States.

Anesthetic and surgical complications:
Age, nutritional status, pre-existing medical conditions will all affect risk associated with anesthesia and surgery. Risks associated with surgery include hemorrhage, hypothermia (chilling), pain, wound infection or breakdown of the incision line, delayed wound healing and death. Complications rates among veterinary students reach 20-30% and most of these are considered minor complications. Complication rates for graduate veterinarian are considerably lower. Complications can be reduced by careful patient selection, safe pre-anesthetic and anesthetic protocols, good surgical techniques, careful anesthetic and post-op monitoring, and effective multimodal pain management both pre and post-op.

Conclusions:

While gonadectomy is generally accepted as the standard in the United States, it is important to consider all the factors that may affect a particular individual animal and their risks. While it still appears evident that gonadectomy is considered beneficial, the age at which animals are neutered is currently being reconsidered. Certainly for animals relinquished to shelters or rescue organizations, gonadectomy is best performed prior to release to the new owners. This will ensure that these animals that have already been relinquished once or have been free-roaming will never become pregnant or cause another pregnancy. For animals in the general population, a full discussion with your veterinarian is recommended to determine when and if each pet should be spayed or neutered.

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