Neoplastic conditions associated with spay/neuter status in the canine
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Neoplasia, including malignant and non-malignant tumors, represents the single most important group of diseases in both veterinary and human medicine today. Recent studies have shown that cancer is the cause of death for 15-30% of dogs and 26% of cats. As a consequence, a large body of research focuses on the causes, diagnosis and treatment of this diverse group of conditions.

As the study of cancer in pets evolved, it was quickly recognized in the 1960’s that some cancers were related to the presence or absence of a dog’s reproductive tract. A series of studies demonstrated that vaginal tumors, uterine tumors, ovarian tumors and mammary tumors could all be substantially reduced or eliminated by removal of the ovaries and uterus or of the ovaries alone.1,2 As a consequence of this work, and the wide-spread adoption of spay-neuter programs in the USA, these tumors represent a very small percentage of disease in this country. In contrast to this, mammary tumors represented the most common tumor submitted for histopathology in a Norwegian study. Mammary tumors accounted for 30% of submissions - approximately 9-13% of dogs - and 94% were malignant or pre-malignant based on modern criteria.3 Separately, mammary tumors were among the two main reimbursement claims in female dogs (the other was pyometra) in a recent Swedish study.4

However, while this stark difference may be interpreted as a success for US veterinarians, recent studies in regard to other tumors have demonstrated that ovariohysterectomy has the opposite effect on a number of other important tumors, including osteosarcoma, hemangiosarcoma, cardiac tumors, mast cell tumors and lymphoma.5-11 These data are widely available to owners and veterinarians and may be a source of confusion and frustration to both veterinarians and owners considering gonadectomy. There is an urgent need for veterinarians to develop scientifically sound recommendations that are sufficiently nuanced to educate owners and guide them in a decision-making process regarding their animal. There is further an urgent need for veterinarians to be prepared to discuss the benefits and risks of surgical gonadectomy with public interest groups and policy makers in order to serve as effective advocates for animal and human welfare in the USA.

Only mast cell tumors approach the incidence of mammary tumors, accounting for 16-21% of cutaneous tumors (approximately 2.5-3% of dogs) in several studies from the USA,7 and 3-11% of tumors across all age groups in Norway.3 Across all breeds, the other tumors discussed affect a very small proportion of dogs (0.2-1% each).

However, within specific breeds, the risk of developing specific tumors can be substantially higher. In Rottweilers, the incidence of osteosarcoma has been reported between 12-25% and the relative risk of diagnosis with mammary tumors or osteosarcoma was 100:1144, according to Gamlem and co-workers.3,5-6 In contrast, the relative risk of the same tumors on the Dachshund was 194:73.3 In addition to this source of variation, there are two other major sources of variation based on tumor type: differences in gender predilection toward tumors, and differences in response of tumors to ovariohysterectomy/neutering. In regard to the latter, mammary tumors are dramatically more common in female dogs than male dogs, and there is convincing evidence that removal of the gonads early in life results in the greatest reduction of tumor development (95%), with decreasing benefits as the animal ages to approximately a 25% reduction in tumor development after the third heat.12-14 In contrast, delaying ovarian removal beyond 1-4 years of age attenuates the increased risk of osteosarcoma in spayed Rottweilers.5,6 A third response pattern for tumor-development is seen with several other tumors. Several studies have shown an increased risk for hemangiosarcoma and mast cell tumor in dogs spayed after seven to 12 months, compared to either dogs spayed early or intact dogs, whereas the effect of age at spay has been variable across breeds for lymphosarcoma.10,11

These complicated relationships between gender, gonadal status, breed and tumor risk need to be addressed through proactive conversations between owners and veterinarians. The primary factors that should be accounted for when deciding if and when to perform a spay/neuter procedure are:
- Owner’s willingness to accommodate for normal reproductive physiology and behavior, and the owner’s ability to prevent unwanted breedings.
- Breed of dog
- Breed predisposition to development of specific tumor types or other complications
- Relative morbidity/mortality associated with specific tumor types

Other factors that should also be taken into consideration are:
- “Family history” of lines within a given breed in regard to conditions known to be related to spay
- Purpose of the dog
- Health status of the dog prior to surgery

Unfortunately, in many cases, insufficient information is available to make clear recommendations for different breeds. Even when information is available, it is often incomplete, or the research is subject to bias based on study design and the limitations of retrospective research. In addition, differing statistical terminology and methods complicate interpretation of data across studies. As a consequence, it should be understood that in many cases a recommendation can only be made based on clinical experience, extrapolation from better-studied breeds and with significant input from owners. Generalizations, both by the veterinary community and by breeders/owners may not prove accurate as research in this field evolves and may cause significant harm to individual animals. They should be used only as a starting point for discussion. In the Table is a broad summary of relative risk for common tumor types and effect of neuter on the incidence.

Table. Summary of relative risk for common tumors.

<table>
<thead>
<tr>
<th>All Breeds</th>
<th>Mammary tumor risk/risk for malignancy</th>
<th>Bone tumor risk</th>
<th>Vascular tumor risk</th>
<th>Lymph tumor risk</th>
<th>Cutaneous tumor risk</th>
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<tbody>
<tr>
<td></td>
<td>9-25% intact; 50-94% malignant; 0.3% intact; 98% malignant</td>
<td>0.3% intact; 87% malignant</td>
<td>0.3% intact; 100% malignant</td>
<td>0.3% intact; 15% intact; ~1% MCT</td>
<td></td>
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<tr>
<td>Effect of spay-status</td>
<td>25-95% reduction in tumor dev. 1.3-5 fold increase 2-9 fold increase 2-4 fold increase (MCT)</td>
<td>2-4 fold increase</td>
<td>2-4 fold increase (MCT)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extrapolated risk in spayed animals</td>
<td>0.9-6% 0.4-5% 0.6-2.6% 0.6-1.2%</td>
<td>0.9-6% 0.4-5% 0.6-2.6% 0.6-1.2%</td>
<td>0.9-6% 0.4-5% 0.6-2.6% 0.6-1.2%</td>
<td>0.9-6% 0.4-5% 0.6-2.6% 0.6-1.2%</td>
<td>15-20%; 4% MCT</td>
</tr>
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Additional information about relative risk of disease among breeds is not readily available from any source. Specific retrospective studies have now been completed on some tumors for the Rottweiler, Golden Retriever and Vizla in the USA, while Gamlem and co-authors described the relative risk of tumor development among breeds in Norway. Together with this, veterinary experience and knowledge of historical disease within a line of dogs can guide a decision-making process to determine when or whether to neuter dogs. Across breeds, removal of ovarian hormones has a strong benefit of reducing the lifetime risk of mammary tumors and pyometra. These conditions affect a large proportion of un-spayed females (mammary tumors 13% by age 10, pyometra 19% by age 10) and are associated with mortality of 50% or higher. Within breeds, the incidence of specific tumors, as well as other conditions affecting animal health, may outweigh this benefit. To exemplify this, two breeds in which recent research has characterized the relative tumor risks are discussed below:

In Vizlas (breed specific risk for mammary tumors was not reported), the frequency of reported cancer was 24% of animals, with frequencies of 5.9%, 2.8% and 1.8% for mast cell tumor, hemangiosarcoma and lymphoma, respectively. The risk for each of these specific
tumor-types was elevated in spayed animals and the onset of cancer in general was earlier for spayed animals. Cumulatively, the risk for these tumors, which may have a higher mortality and earlier onset than mammary tumors, may outweigh the risk of mammary tumor development in intact Vizlas. Furthermore, the tumor-types studied in this breed appear to be most common after delayed ovariohysterectomy or castration. Thus, recommendations to delay sterilization beyond the first heat or first year of age may not be beneficial. To be able to make a sound recommendation, the breed-specific risk for mammary tumors should be assessed.

In Rottweilers, the risk of dying due to osteosarcoma is as much as 2x higher than the risk of dying due to mammary tumors. Furthermore, benefits of ovarian hormones for tumor prevention have been recognized up to one to four years of age whereas pyometra and mammary tumors commonly are seen after that age. Thus, animals can be spayed prior to the most common onset of reproductive conditions and after benefits of ovarian hormones have had an effect. This approach will reduce the likelihood of an animal developing pyometra, provide some (25%) reduction in development of mammary tumors, while maximizing the preventive effect of ovarian hormones of osteosarcoma development.

In conclusion, it is increasingly recognized that the approach of “individualized medicine” is particularly important in regard to a question that was long considered settled among the veterinary community, namely whether animals benefit from surgical sterilization. As researchers expand the body of knowledge, easy answers may not be readily available and a recommendation to spay or castrate should be made after consideration of health-risks associated with specific breeds or lines of dogs, and in conversation with the owner.

References