

Can We Neuter Cancer in Dogs?

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I spent this past month reviewing studies reported over the past 30 years regarding the role of hormones and cancer in dogs.

Do neutering and spaying increase or decrease the risk of cancer?

Do the procedures alter the prognosis once a pet develops cancer? How do hormones cause or prevent cancer?

Uncertainty Factor

I'm still not sure what to recommend to my clients.

There are reports showing that spayed females have four-time greater risk for developing cardiac hemangiosarcomas compared to intact females. Neutered males also show a significant increase in risk for these tumors compared to intact males.

Many of us are familiar with the data that show that female dogs spayed before the first heat cycle have half the risk of mammary carcinoma of those spayed after the first cycle but before the second heat cycle. Dogs spayed after the fifth heat cycle, or never spayed, have the highest risk.

Testicular carcinomas in dogs are common, but neutering eliminates that risk.

But prostate cancer is actually more common in castrated dogs than intact ones. Prostate cancer in dogs is hormonally independent and castrated dogs have up to a four-time greater risk of developing prostate cancer than intact dogs.

Neutered or spayed dogs have a one-half to threefold higher risk for developing bladder tumors and twice the risk of developing osteosarcoma as compared to intact dogs.

In one study, males were four times more likely than females to die within two years of diagnosis. Male and female dogs that underwent gonadectomy before 1 year of age had an approximate one in four lifetime risk for osteosarcoma and were significantly more likely to develop a tumor than dogs that were sexually intact.

Hormones' Role in Cancer

The possible mechanism by which gonadal hormone exposure might protect against or cause the development of tumors in both males and females is not known.

Endogenous sex steroids such as estrogen and testosterone may serve as prodifferentiation agents that inhibit the malignant transformation of cells.

Alternatively, gonadectomized female and male dogs live longer than sexually intact

dogs, which might be expected to contribute to a higher overall cancer incidence associated with gonadectomy reported by others.

There are substantial and convincing bodies of experimental, clinical and epidemiologic evidence indicating that hormones play a major role in the etiology of many cancers.

The underlying mechanism proposed is that neoplasia is the consequence of prolonged hormonal stimulation of the particular target organ, the normal growth and function of which is controlled by one or more steroid or polypeptide hormones.

Genetic Controls

Evidence is mounting to show that the amount of hormone to which a tissue is effectively exposed is under strong genetic control.

Therefore, in addition to external factors such as diet or exogenous hormone use, which may modify hormone profiles, polymorphisms in genes encoding proteins involved in steroid-hormone biosynthesis, metabolism or extra- and intracellular transport and DNA binding are important determinants of individual cancer risk.

The major carcinogenic consequence of this hormonal exposure and the end organ is cellular proliferation.

The emergence of a malignant phenotype depends on a series of somatic mutations that occur during cell division, but the entire sequence of genes involved in progression from normal cell to a particular malignant phenotype are not known.

Candidate genes include those in the endocrine pathway as well as DNA repair genes, tumor suppressor genes and oncogenes.

One explanation of why hormones may initiate cancer but then the cancer progresses in a hormone-independent environment is discussed in the June issue of Nature Medicine.

Dr. David Feldman found that, because of a mutation, the stress hormones cortisone and cortisol can trigger the growth of later-stage cancer cells. Feldman and colleagues report that an androgen-receptor gene in metastatic cancer cells contains two mutations that transform its activity.

Androgens are no longer bound tightly to the receptor. Instead, cortisol and cortisone bind and act like pseudo-androgens, activating the same metabolic pathways that androgens normally would trigger.

This means that cancer cells are deluged with signals to divide, which could account for their rapid multiplication in high-grade metastatic or later-stage cancers.

So do we neuter dogs at an early age to prevent breast and testicular cancer but place

them at risk for hemangiosarcomas, osteosarcoma, bladder or prostate cancer?

Do we monitor cortisol levels in dogs with cancer and attempt to reduce these levels in order to improve prognosis?

Unfortunately the answers are not known, but are close at hand.

With the development of the canine genome map, investigators are able to identify loci that predispose dogs to cancer.

My hope is that this will lead to an understanding of gene regulation and the role of hormones in cancer initiation and promotion. Then, and only then, will we know when it is time to neuter cancer.

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