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Center for Companion Animal Health
UC Davis School of Veterinary Medicine

By learning more about canine cancer, owners may be able to assess whether their dog could be at risk, and what they might be able to do to reduce the chances that their dog will be affected.

Special Report:

Understanding Canine Cancer

By Rhonda Hovan

Just as it is in people, cancer is one of the leading causes of death in dogs. It's estimated that approximately one in three dogs will get cancer, which is very similar to the rate of cancer in humans. This increases to about one in two dogs over the age of ten. Clearly, cancer is a major concern to all who love and care for dogs.

Any dog can develop cancer, but some dogs are at greater risk of doing so than others. Sometimes this elevated risk is related to the breed of dog, and sometimes lifestyle factors can modify a dog's cancer risk. By learning more about canine cancer, owners may be able to assess whether their dog could be at risk, and what they might be able to do to reduce the chances that their dog will be affected.

Defining Cancer

First, it is important to understand that cancer is not a single disease, but many diseases that share certain characteristics. The predominant characteristics are that cancers contain cells that don't stop multiplying when they are supposed to and cells that don't die when they are supposed to.

Cancer can arise from many different types of cells, and its cell of origin gives a cancer its identity and unique characteristics. For example, one of the most common canine cancers, lymphoma (also called lymphosarcoma), arises in a type of white blood cell called a lymphocyte. A cancer that usually occurs in larger breeds, osteosarcoma, begins in bone cells; and as the name implies, mast cell tumors—common tumors that usually appear on the skin—arise from mast cells.

One cancer that is often confusing is hemangiosarcoma. This cancer forms from cells called endothelial cells that line blood vessels. Typically, hemangiosarcoma tumors form in very vascular organs such as the spleen, liver, right atrium of the heart, and lungs; but they can form in almost any organ, including the brain and skin. However, no matter where the primary tumor is found, it is not a "spleen cancer" or "liver cancer" or "lung cancer" if the tumor cells are endothelial cells. Attending veterinarians usually rely on a pathologist to examine cells from the tumor to identify the type of cancer.

Cancer as a Genetic Disease

So what causes a cancer to form? Veterinarians and scientists know that cancer is a genetic disease. But to dog owners and breeders, the word "genetic" does not necessarily mean the same thing that it means to cancer researchers. When scientists use the word genetic, they mean that they always need to look at genes to understand what has gone wrong to cause a cancer to form, because it is errors in genes that allow cells to multiply without normal controls.

But just because cancer is a genetic disease does not mean that it is strictly an inherited disease. So how can it be genetic and not be inherited? This is because genes are found in two kinds of cells, and one kind is inherited and the other kind is not. The kinds of genes most owners and breeders are used to considering are found in germ line cells, which are the sperm and the egg. These are the cells that contain genes that are passed on to the next generation. All other cells of the body are

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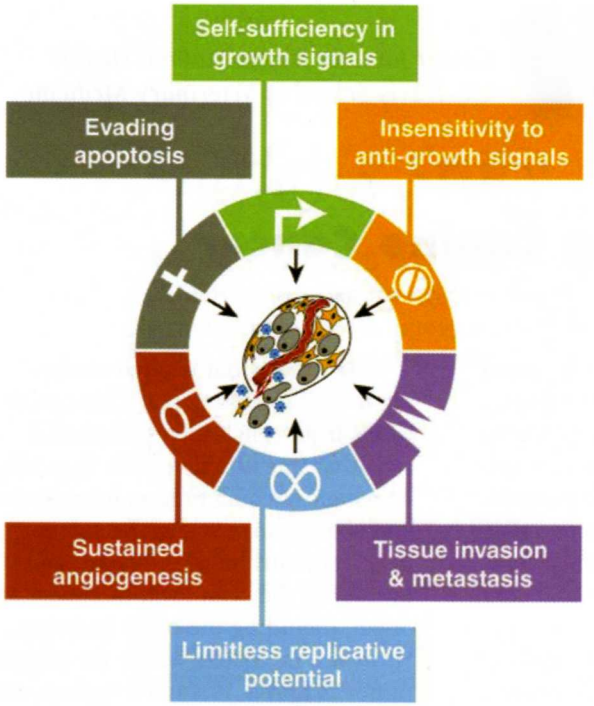
Ms. Hovan is the research facilitator for the Golden Retriever Club of America and founded the Starlight Fund at the AKC Canine Health Foundation to support Golden Retriever health research. She also serves on the advisory board of the National Canine Cancer Foundation, and is an emeritus director of the Orthopedic Foundation for Animals. She lives in Akron, Ohio, with five Goldens and two rescued raccoons. She can be reached at RhondaHovan@aol.com.



Acquired Capabilities of Cancer

For a normal cell to become a cancer, it must undergo the following changes:

- It no longer responds to all external signals that control its growth (self-sufficiency in growth signals)
- Ignores normal external signals to stop growing (insensitivity to anti-growth signals)
- It must be able to invade other tissues where it wouldn't normally grow (tissue invasion & metastasis)
- It becomes immortal (limitless replicative potential)
- It must be able to attract its own blood supply (sustained angiogenesis)
- It ignores signals telling it to commit suicide (evading apoptosis)

Figure 1. Modified from Hanahan & Weinberg, "The Hallmarks of Cancer," *Cell*, 100: 57–70, 2000 Elsevier, U.K.

called somatic cells. They also contain genes, but the genes in somatic cells are not passed forward and can have no effect on the next generation. Any mutations that might occur in somatic cells during the lifetime of the animal are confined to that one animal and cannot affect its offspring.

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So errors in genes lead to cancers, and those errors are called mutations. Every time a cell divides, it must make a copy of its genes for the new cell, and that copying process provides an opportunity for a mistake. Most of the time, the mistakes are either corrected, eliminated or are harmless; but every now and then, a mistake that impairs the normal function of a gene will be maintained. Fortunately, very few cancers are the result of a single mutation, and essentially all common cancers in dogs require numerous genetic errors. This is called the multiple hit theory of cancer (Knudson A, 1971), and applies to humans as well as dogs. It's estimated that cancers require at least five to six meaningful mutations to gain a foothold, and probably more.

These mutations can occur in germ line cells—the sperm and the egg—and they can occur in somatic cells. And it is most likely that the mutations leading to cancer come from a combination of germ line cells and somatic cells. Therefore, it is most accurate to say that cancer in dogs is partially inherited, and partially not inherited. Neither inheritance by itself nor environmental exposures by themselves cause cancer in dogs; but both contribute to cancer in dogs. Inherited mutations can be the first steps toward cancer, giving a puppy the predisposition to develop cancer—but the next steps occur during the life of the dog, and are not influenced by heredity. This predisposition toward cancer certainly does not mean that cancer is inevitable, and many predisposed dogs will live long lives with no cancer.

The basic steps necessary for a cancer to grow are defined in the IPP model—initiation, promotion, and progression (Trosko JE, 2001). In the initiation phase, a cell is endowed with immortality or another growth or survival advantage, but is still held in check by its cellular environment. This step is particularly intriguing, because some very new research is pointing toward the strong possibility that this immortality can be an inherited component of cancer, and is part of the "cancer stem cell" theory. During the next step, promotion, additional mutations allow the cell to out-compete neighboring cells, and a tumor mass is formed. Finally, progression occurs when a third series of mutations leads to metastasis. Each of these steps is achieved through multiple mutations.