

# Large-Scale Cancer Study of Golden Retrievers Holds Hope For All Dogs

On the trail of canine cancer

By  
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In *Dog Diseases Treated by Homeopathy* (first published in 1863, before chemotherapy, radiation, biopsies and blood panels), author James Moore advised concerned dog owners on treating cancer: “An operation cannot remove the cancer, but it can remove the tumor, which causes much suffering; the knife is, therefore, merely palliative in its effect. Still, the disease, even then, is likely to return at a period more or less remote.”

Today, the diagnosis isn't as bleak. Indeed, 50 percent of all canine cancers are curable if caught early enough. Moreover, the disease is mostly an affliction of old age (tragically, some cancers strike dogs as young as two). It may seem like more dogs get cancer than ever before, but it's presumably because they enjoy a longer life span, thanks to vaccinations against infectious diseases like parvovirus and distemper, and new treatments for congenital, degenerative and metabolic disorders.

“Cancer” is the broad term for a complex cluster of more than a hundred diseases. Although there are many causes, each type of cancer starts with alterations in genes that tell cells how to function, which triggers accelerated and uncontrolled cell growth. The defective signal may hide in abnormal genes inherited from

parents, or germinate when normal genes are exposed to harmful environmental influences.

Some breeds are predisposed to certain types of cancer, and in those cases, a strong inherited genetic component is suspected. It is thought that a small number of genes account for cancer risk, but, although they are directly related to the development of individual cancers, rarely is a single gene the sole cause.

By the time people and dogs pass 70 and 10 years of age, respectively, about 50 percent will have been diagnosed with some type of cancer. The malady accounts for approximately 23 percent of all deaths in people.

In dogs, cancer mortality varies across breeds, from under 10 percent to higher than 60 percent.

In general, small dogs weighing less than 20 pounds are at very low risk. (Small dogs have lower levels of IGF-1, a hormone that is related to bone and tissue growth. Researchers suspect this may be one reason they have a lower incidence of cancer.) For instance, the chance that a Chihuahua, Dachshund, Maltese, Miniature Pinscher or Pomeranian will get cancer is less than 10 percent. Breeds with the highest risk include the Bernese Mountain Dog, Bouvier des Flandres, Boxer, Bullmastiff and Golden Retriever (Fleming et al. 2011).

#### **Goldens as Case Studies**

The high incidence of cancer in Golden Retrievers appears to be a relatively recent phenomenon. Although the breed was neither over- nor under-represented in a 1988 health study conducted by the University of Pennsylvania School of Veterinary Medicine (Prymak et al. 1988), a health report published 10 years later by the Golden Retriever Club of America (GRCA) identified cancer as the cause of death in 61.4 percent of their dogs (Glickman et al. 1999).

Interestingly, cancer risk in Europeanbred Goldens appears to be significantly lower. A 2010 study put the mortality figure at 38.8 percent (Dobson 2012, Adams et al. 2010). Although much higher than average, the incidence is substantially lower than that found in North American Goldens.

Goldens in Europe and the U.S. may look similar, but there are enough DNA differences to separate the dogs into two distinct populations corresponding to their geographic regions. Gene pools on both continents are large, so breeding between the two populations is rare.

When studied in the lab, genomic differences suggest that risk for some types of cancer is related to recent genetic mutations in North American Golden Retrievers. And this could be good news: genetic differences between European and North American Golden Retrievers may be key to understanding the etiology of canine cancer overall.

#### **Population, Popularity and Popular Sires**

The Golden Retriever is a relatively modern breed, developed in Scotland in the mid 19th century and registered in the UK in 1903, about the same time the dogs were imported to the U.S. In 1925, Goldens were

registered with the American Kennel Club, and by the 1950s, the affable sporting breed had gained popularity in this country. Today, they are the third most popular breed in the U.S., with the AKC reporting about 42,000 registrations, a small fraction of the total number of Golden Retrievers living in this country. In the UK, Golden Retrievers rank eighth on the popularity chart, with 8,000 registrations.

Registration agencies impose strict standards on pedigreed dogs, requiring that the ancestors of each dog be registered as well. This, combined with widespread use of popular sires, means that each breed is a closed population, with no gene flow. The “popular-sire” effect occurs when an animal with desirable attributes is bred repeatedly. Descendants share specific genetic mutations, both good and bad, and those mutations spread rapidly throughout the gene pool, where they may become permanently established, or fixed. (“Fixation” is a change in a gene pool in which at least two variants of a particular gene are reduced to only one.)

When the 1998 GRCA study confirmed that a high number of Golden Retrievers were dying of cancer, club members realized they had both a problem and an opportunity. The club’s nonprofit 501(c)(3) fundraising offshoot, the [Golden Retriever Foundation](#) (GRF), got off the ground about the same time the survey results were being analyzed.

It started by funding a few cancer studies, including some managed by [Morris Animal Foundation](#) (MAF), a nonprofit that invests in science to advance animal health worldwide. Eventually, GRF contributed \$1 million and asked MAF to match it if both could agree on a project.

In the meantime, at a MAF canine cancer summit in Chicago, three goals were promulgated: build a tumor archive, fund more canine cancer studies and devise prevention strategies. In response to this collaborative effort, a team of scientists, epidemiologists, veterinary oncologists and surgeons, nutritionists, toxicologists, geneticists, breeders, and donors spent three-and-a-half years designing the ideal study. Not an easy task.

Animal epidemiology studies (which deal with the incidence, distribution and possible control of diseases) are few in number, largely because they face so many obstacles. Among them are limited funding, participating private practices using non-standardized methods to record data, pedigrees that are difficult to confirm, and grieving owners who aren’t eager to authorize post-mortem tests. Some cancers are silent killers, so a sudden death may not be attributed to cancer. And, due to attrition, studies are difficult to adequately enroll and don’t last long enough to develop statistically significant patterns.

However, after almost four years of stops and starts, the [Morris Animal Foundation Golden Retriever Lifetime Study](#), the first breed-specific, life-to-death research project of its kind, was launched on August 30, 2012.

### **The Study**

Between 2012 and 2015, MAF enrolled 3,000 dogs ranging in age from six months to two years. Researchers

anticipate that within this population, some dogs will get cancer while others will remain cancer-free. Interested Golden Retriever owners completed questionnaires, then met with veterinarians who did physical exams and collected noninvasive biological samples, a process that the owners committed to having repeated annually during the lifetime of each enrolled dog.

Based on observations summarized in questionnaires, researchers hope to identify potentially modifiable risk factors that may account for the high incidence of cancer and other diseases in Golden Retrievers and, eventually, in all dogs. Funded and managed by MAF, the study will investigate the effects of genetics, nutrition and exposure to environmental factors.

Although other breeds are at higher risk for cancer, Golden Retrievers were chosen because their population exceeds that of most other breeds by a large margin: the larger the sample size, the more accurate the data. Additionally, because these versatile dogs perform multiple jobs—from assistance and search-and-rescue work to field, performance and companion tasks—they are subject to a broad range of environmental exposures.

Rodney Page, veterinary oncologist and director of Colorado State University's [Flint Animal Cancer Center](#) and the project's principal investigator, describes some of the factors underlying the study. "Within the estimates that we currently have, we know that 50 percent of canine cancers are curable with surgery and other treatments. Our study is addressing the ones you can't cut out: the 15 percent of mast cell tumors that aren't operable; lymphoma, a whole-body cancer; osteosarcoma and hemangiosarcoma, because they spread rapidly before they're discovered. These four types of cancer cause approximately 80 percent of cancer deaths in Golden Retriever dogs." These fatal cancers begin to increase in incidence around five to six years and peak about age nine or ten. However, they may also develop in dogs age two and younger.

More than 2,050 veterinarians are providing health care for enrolled dogs. Annually, they conduct physical exams and report findings online; collect samples of blood, urine, feces, hair and toenail clippings and send them to participating laboratories; submit health information from additional health visits; collect tumor tissue samples when applicable; and provide owners with information and guidance to help them make a choice about necropsy (an autopsy performed on an animal) after the dog dies.

Participating veterinarian Stephanie Ensley of Bentonville, Ark., who enrolled her own Golden in the program, elaborated on the study's intent. "The information we'll gather looks at areas of potential exposure by air, contact and feeding. Owners are expected to provide information as detailed as chemicals used in the home, yard and on the dog, and drinking water sources, to name just a few. When all this information is put together and analyzed, we'll have an opportunity to find commonalities that may be related to cancer and other diseases. The more data available, the more opportunity to find a connection. On the flip side, we'll also find commonalities in dogs who live to be 15 and over."

Among the study's other expected outcomes are insights into how dog-breeding practices and lifestyle choices might be modified to reduce the prevalence of myriad diseases, and the creation of a repository of biological samples that may be made available to researchers working to develop genetic tests.

### **Possible Solutions**

Appropriate canine candidates for the study were, in large part, identified through the [Golden Retriever Club of America](#), whose membership represents diverse interests and geographic distribution.

As GRCA research facilitator and breeder Rhonda Hovan, who has been a Golden Retriever advocate for 45 years, notes, "Breeders play a special role in the success of the study because they can recruit multiple siblings who share the same genetic heritage. Data from littermates who experience different environmental factors and diets during their lifetimes may provide unique scientific insights that could make a significant impact on the long-term health of dogs."

One immediate benefit is that veterinarians, dog owners and dogs won't have to wait until the study is complete to see results that may help influence and improve veterinary medicine. The questionnaire responses are analyzed quarterly, so information is continually streaming into the study, and trends, once validated, will be published as they emerge.

Genetic testing to eliminate dogs from the breeding pool may not be the panacea it first appears. Dogs share more the 300 inherited diseases with humans, from narcolepsy and hemophilia to diabetes and lupus. It's unlikely that all of these can be bred away from while still maintaining healthy genetic diversity. Reducing diversity increases risk for other diseases to surface in the future, especially in a breed like the Golden Retriever, one that has already experienced diversity loss caused by widespread use of popular sires.

In an article published in [Golden Retriever News](#) (Nov/Dec 2014), Hovan cautioned Golden Retriever breeders: "Keep in mind that when we remove a dog from breeding due to a failed health test or for any other reason, we are removing all of that dog's genes from the gene pool, not just the genes associated with disease or unwanted traits ...". She also observed that rigorously removing dogs affected with minor conditions has far more potential to damage future generations than occasionally and carefully breeding them. Breeding away from targeted conditions, she says, is part of an inescapable loop that presents subsequent generations with an elevated risk of having some other problem arise. "When conditions are targeted without good cause, there's an all-too-real possibility that the 'something else' will be worse than whatever it is we tried to breed away from to begin with."

Eliminating dogs based on genetic tests is not a sustainable way to control disease. A better approach, Hovan explained, is to "test and replace" as opposed to "test and eliminate." For diseases with a recessive mode of inheritance, breeders can avoid risk by breeding carrier and affected dogs to normal dogs. That way, the

genetic variety represented by the line can be maintained for as many generations as it takes to arrive at genetically normal offspring.

As Hovan went on to say, “To make good decisions as caretakers of our breed, we need to know what we’re working with. You can’t change what you don’t measure.” To this end, GRCA is working with a research team from University of California, Davis, to survey the breed’s genetic diversity across types and geographic location, collecting samples from the U.S. and Canada. Referencing this survey, Hovan added, “We want to approach this in a scientific manner. This study will help to clarify what we need to do and provide a road map so we can move forward.”

Could one solution be as straightforward as avoiding environmental triggers that trip biological switches and activate uncontrolled cell growth? Maybe. Researchers expect to collect enough biological samples to accurately define the incidence of each cancer being studied. When the study ends, researchers will also have a detailed life story of every enrolled dog. The hope is that in the long run, data will show relationships between cancers and exposures.

The population-based study is creating a baseline for future research in all sorts of health-related issues. According to Page, “The samples and data we are collecting now will be used by scientists in the future to answer their own questions about health and wellness issues in dogs. Studies will be encouraged that access these assets for analyses of everything from toxic exposures to microbial populations in the gut as they might influence health outcomes.”

Cohort studies like the Golden Retriever Lifetime Study are costly, susceptible to attrition and take a long time to produce statistically useful information. Their value depends on an organization’s capacity to stay in touch and engage all participants. DVM, PhD and CEO of Morris Animal Foundation David Haworth, who also enrolled his dog in the program, summarizes it most concisely: “A study like this can only happen through the active participation of an extended community of dog owners, dogs, veterinarians and study sponsors. I think I can say with absolute certainty that we have one of the most active groups of study subjects of any longitudinal health study ever initiated. After all, they are Golden Retrievers.”

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*The Morris Animal Foundation Golden Retriever Lifetime Study is estimated to eventually cost \$25 million; at this point, MAF is \$7 million short of the goal. Major donors include the Morris Family Foundation, Petco, Zoetis, VCA Antech, Mars Veterinary and the Hadley and Marion Stuart Foundation. To learn more, visit [caninelifetimehealth.org](http://caninelifetimehealth.org).*

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