

THE FUTURE OF THE 'C' WORD

Cancer, Canines and the Human Connection

By Rachel Brix, CPDT-KA



◀ A Pit Bull is dressed in a tutu for cancer awareness.

“Dogs’ lives are too short. Their only fault, really.”

– Agnes Sligh Turnbull

The anniversary of my heart dog’s passing looms as I write this piece. When Percy went to the Rainbow Bridge on July 11, 2011, she had lived more than two years with cancer; probably longer if you factor in how long she may have had it before we knew she had it. In her adolescence, my father had nicknamed her “The Percinator,” or “Nade” for short, for her insatiable hobby of killing small animals on our 26 acres. But Nade couldn’t kill the malignant nerve sheath tumor that grew on her torso. We couldn’t kill it with surgery; it grew back faster than anyone anticipated. After Nade’s surgery, we kept T-shirts on her to help protect the wound. And I suppose we did it also in a vain attempt to hide it; maybe if we couldn’t see it, she wouldn’t really have cancer.

It’s rare to find someone who hasn’t experienced loss of a human or canine to cancer, more than likely we’ve grieved both. According to the Animal Cancer Foundation, 6 million new canine cancer diagnoses are made annually (out of 65 million dogs), compared with 1 million human cancer diagnoses (325 million people in 2017). One in three people will get cancer, compared with 50 percent of dogs age 10 or older. Dogs and humans don’t just share family-type bonds and sometimes even our beds, they also share many of the same cancers and respond to the same treatments. Research as to causes and treatments is making headway, and the similarities between human and dog cancers have prompted increased comparisons, benefitting both canine and human alike.

Comparative Oncology - A New Leash on Life

Comparative oncology is a newer yet rapidly expanding field that aspires to find effective treatments for cancer in pets, that may produce innovative treatments for humans. Consequently, the research gives pet parents access to unconventional and novel therapies while serving as models for human treatments, a win-win.

Since the goal is to advance both canine and human health, comparative oncology is an interdisciplinary and collective effort of doctors, veterinarians, oncologists, biologists and many others from a variety of medical centers and universities. The focus is on the relationship of cancer as it presents in both dogs and humans; and since its manifestations are similar, the theory is treatments can be, too.

A partnership collectively known as the Comparative Oncology Trials Consortium (COTC) is a network of 20 academic veterinary oncology centers. This alliance is managed by the National Cancer Institute's Comparative Oncology Program (COP) that is part of the National Institutes of Health (NIH). The COP “designs and executes clinical trials in dogs with cancer to assess novel therapies ...and integrate[s] them into the design of current human Phase I and II clinical trials,” according to the American Cancer Foundation's website (www.acfoundation.org).

Because dogs get so many of the same cancers humans do, dogs make ideal models for study. “Spontaneous cancers in dogs and cats are an underused group of naturally occurring malignancies that share many features with human cancers, such as osteosarcoma, prostate and breast cancers, non-Hodgkin's lymphoma, melanoma, soft tissue sarcoma, head and neck carcinoma, and virally induced lymphomas,” the National Cancer Institute explains.

Comparative oncology was born, in part, out of frustration with some of the animal models; therefore, many researchers have become more interested in studying dogs than mice. For one, dogs get cancer spontaneously, as do humans. On the other hand, mice do not — they must be purposely infected with it — and their immune systems are often altered, making them inadequate subjects for reliable studies, especially when it comes to immunotherapy.

In an interview with the hematology/oncology magazine *HemOnc Today*, Arta M. Monjazeb, MD, Ph.D., associate professor in the department of radiation oncology at University of California Davis declares, “The more research we are conducting, we are finding that they [dog cancers] represent human cancers very closely. They grow very similarly, they metastasize very similarly, and their histology and genetic landscape is very similar. Their responsiveness to drugs is also very similar.”

Considering the modern boom of the pet industry and our willingness to provide for our pets, we are also more likely to explore various treatments for our dogs when they get cancer; therefore, we're more willing to be a part of trials for innovative advancements. By studying and researching pet dogs as they compare to humans, science stands to forge a positive relationship between humans and animals that will provide mutual benefits.

Connecting the Treatment Dots

Traditional and typical treatments for cancer include surgery, while chemotherapy and radiation are regularly used in combination. Surgery is often the best-case scenario if the tumor can be excised cleanly; however, it is often difficult and sometimes not feasible. And then there's the possibility the cancer has metastasized.

In Percy's case, the tumor had such a stranglehold on her insides that clean margins were impossible.

Chemotherapy, or chemical therapy, attacks cancer cells; however, it unfortunately also attacks healthy cells, oftentimes compromising the immune system. While it can sometimes add months to a dog's life, it rarely results in remission. Many pet parents are reluctant to subject their pet's quality of life to the potential side effects during their final months.

Radiation treatment can also be effective to control or even shrink tumors; like chemotherapy, however, radiation can attack healthy cells and interfere with the ability to heal. Moreover, radiation is often very time consuming and potentially stressful for an ailing dog, usually requiring three treatments per week for four weeks. It's also expensive, and frequently must be paired with another treatment type. A modern alternative to radiation, photodynamic therapy (PDT), directs a laser precisely at the tumor, which is less invasive for the dog, less time-consuming (usually just one visit) and generally less expensive. However, its efficacy is often limited to superficial tumors.



Percy

Roger Govier, a frequent contributor to the *Whole Dog Journal*, laments in his April 2018 article “Every Approach to Cancer Treatment Has Benefits and Risks: “While research in these areas has brought significant advances, the overall picture is discouraging; cancer death rates are largely unchanged.”

But Govier's outlook isn't all gloom and doom as he lists current research studies on genetic triggers, heredity, hormones, protein synthesis, virology, tumor markers and suppressor genes.

“In the future, this work seems likely to bring about revolutionary advances to all phases of cancer research: Prevention, detection, diagnosis, and treatment. There will be more vaccines against certain cancers (witness the feline leukemia vaccine), protection for those at hereditary risk of cancer, genetic engineering that will predict and control those factors causing cells to mutate, and the ability to identify and screen microscopic cancerous growths, allowing for earlier intervention,” he states.

Considering the development of comparative oncology, the increase of larger and more inclusive studies and the growing number of veterinarians— and doctors— willing to experiment, hope is on the horizon.

Like other vaccines, cancer vaccines attempt to boost the immune system. Uniquely, cancer vaccines are genetically engineered to attack specific features of specific cancers. For example, the University of Pennsylvania's Veterinary Medical School performed a successful pilot study using an osteosarcoma vaccine on an 8-year-old female Golden Retriever named Flyer who was diagnosed in 2015 with bone cancer. She had a leg amputated and chemotherapy, although the cancer generally reoccurs in the lungs within a year. Flyer received three doses of the osteosarcoma vaccine. A year later,

“And for the zillionth time in our 13 years together I told her I loved her. And that someday cancer would be gone for good. Since we all know dogs and humans are good at working together, I finally believe we’re well on our way. “

Flyer received a clean bill of health. Because of positive results, the vaccine went into early human trials afterwards.

Cancer vaccines are intended as a supplement to traditional treatments. Immunotherapy targets the remaining and elusive cancer cells left behind after surgery, chemo or radiation by helping the immune system seek out and destroy them. In 2012, a trial led by Nicola Mason, DVM, at Penn Vet treated 18 dogs who received the same treatments as Flyer: amputation, chemo and three rounds of vaccines. The first patient, Sasha, an American Bulldog, survived almost twice as long as dogs who'd only had the surgery and chemo. Overall, the trial dogs who received the vaccines survived nearly eight months longer than those who had not, with no reported side effects.

Dr. Mason asserts, “This immunotherapeutic approach is very promising as it stimulates the patient’s own immune system to seek out and specifically kill cancer cells that remain after traditional standard-of-care therapy.” The American Cancer Society reports there are now four main types of immunotherapy to augment treatment for certain cancers in humans, and canines have had a big paw in that advancement.

Additionally, gene therapy research continues to look promising, where two different strategies take on two distinctly different paths. One method seeks to alter a body’s immune cells to combat the cancer; the other is to inject cells specifically created to inhibit growth directly into the tumor. According to the Animal Cancer Foundation, “The Canine Genome Sequencing Project at the Broad Institute successfully mapped the genome of a Boxer named Tasha in 2005. The map of the genome has been used to confirm that many of the same genes involved in dog cancers are also involved in human cancers.” And Nicole Ehrhart, VMD, a professor of veterinary medicine at Colorado State University, veterinarian and surgical oncologist, writes on CNN.com, “dogs have greater than 80 percent genetic similarity to humans, versus only 67 percent for mice.” Since dogs are more genetically like humans than mice, comparative

oncology seems poised to make great strides. Dr. Ehrhart goes on to add, “Many of the genetic mutations that drive cells to become cancerous in people are the same mutations that cause cancer in dogs. In fact, when viewed under a microscope, it is impossible to distinguish between a tumor from a human and a dog.”

Another experimental treatment, the brainchild of Dr. Ehrhart, is bone transport, which seeks to replace amputation. Bone transport attempts to eradicate osteosarcoma, the most prevalent bone cancer, by removing the infected portion and replacing it with a healthy segment, thereby retaining the dog’s own matter and blood flow. An “Ilizarov Brace” (named for Russian doctor Gavriil Ilizarov) holds the bone in place as it heals. The healing process is much like that of a fracture, and the brace is adjusted as needed as the limb regains its stamina.

Meanwhile, as research continues to gain ground, canine parents and humans alike are still searching for existing treatments. As a result, alternative treatments have seen a dramatic increase in popularity. According to the website The Truth About Cancer (thetruthaboutcancer.com), a Canadian study found “54 percent of practitioners felt conventional medicine could benefit from the concepts and methods of alternative medicine for the following reasons: most [human] patients were not responding to conventional treatment [and] their patients requested it.” The same can be said for our canine companions—pet parents are looking for sensible and practical alternatives to traditional therapies.

An alternative therapy in the United States is Traditional Chinese Medicine (TCM), used on cancer wards for both human (Harvard Medical School) and animal (Colorado State University's School of Veterinary Medicine). This ancient form of healthcare includes herbal remedies, stress and emotional management, dietary guidance and its signature therapy, acupuncture. Veterinary acupuncture has more than 1,000 vets practicing in the U.S., as well as 17 other countries, according to the American Academy of Veterinary Acupuncture (AAVA). Its website describes that acupuncture "needle[s] specific points, lead[ing] to the release of chemicals in the muscles, spinal cord, and brain. These chemical mediators can change the perception of pain and lead to other chemical mediators that influence organ function. This improved 'chemical communication' stimulates healing."

While there is no claim acupuncture cures cancer, AAVA asserts it can improve quality of life for cancer patients by alleviating associated symptoms such as pain, fatigue, nausea, vomiting and lack of appetite. Human cancer patients undergo acupuncture treatments for the very same relief, and more cancer centers are offering acupuncture as a treatment option. In fact, according to the NIH's journal article "The Value of Acupuncture in Cancer Care," published in August 2008, between 48-to-83 percent of people are turning to complementary and alternative medicine and up to 31 percent have used acupuncture.

As part of cancer treatment, nutrition has also been receiving increased attention. Patients, both canine and human, typically lose weight because the disease compromises metabolism. According to a book co-authored by Greg Ogilvie, DVM, from the College of Veterinary Medicine at Colorado State University, carbohydrates are the main source of dysfunction, essentially robbing the dog of its energy and feeding the tumor instead. Ironically, undiagnosed weight loss often triggers pet parents to increase feeding amounts, thereby potentially contributing, unknowingly, to tumor growth. Research indicates even a dog who goes into remission will still have a compromised metabolism, so proper nutrition is essential. This may include lesser amounts of carbs and sugar, higher amounts of digestible proteins and unsaturated fats, and increased essential fatty acids.

While no clear cancer-fighting diet formula exists, the consensus is that diet is a major contributor to overall health and in moderating disease in both humans and dogs. Much anecdotal evidence also exists, corroborating that diet influences cancer in one way or another. Furthermore, the American Cancer Society (ACS) acknowledges, "Eating the right kinds of foods during and after [cancer] treatment can help you feel better and stay stronger." Therefore, it would also stand to reason diet can help

stave off cancer in the first place, since the ACS also recommends limiting consumption of red and processed meat, eating at least 2 and one-half cups of fruits and vegetables daily, and choosing whole grains instead of refined. It's plausible, therefore, our canine companions—who share the same cancers—could benefit from preventative diet modification as well.

Golden Retrievers May Have Clues to the Cause

"For the most part, dogs get everything we do...You see some striking similarities that you don't see in mice or other animal models, and that makes them an increasingly terrific system to study the genetic basis of disease," affirms Elaine Ostrander, geneticist, distinguished investigator at the National Institutes of Health and chief of its Cancer Genetics and Comparative Genomics Branch (Popular Science, Sara Chodosh, May 1, 2018).

The good news is we don't have to rely on creating, maintaining and testing dog colonies in the unnatural environment of research labs or giving cancer to otherwise healthy animals. We can instead rely on pet dog populations, like the Golden Retriever Lifetime Study of the Morris Foundation. According to its website, the study started as a casual conversation about how "there were no long-term, prospective studies that focused on understanding the genetic, environmental, nutritional and lifestyle risk factors that may be contributing to disease in our dogs – particularly cancer." That conversation evolved into what the Morris Foundation declares as "the largest observational study undertaken in veterinary medicine in the United States."

Launched in 2012, this study follows 3,000 Goldens in each of the 48 contiguous states and has the full cooperation of both pet parents and their veterinarians, and of course, the Goldens themselves. The study, estimated to take as long as 10-12 years, will operate until 500 combined cases of the four primary outcomes (high grade mast cell tumor, hemangiosarcoma, osteosarcoma and lymphoma) occur. As of 2017, the Morris Foundation's website reported, "Of our enrollees, 98 percent remain in the study (unheard of in similar human studies) and 85 percent are compliant with all study tasks." All the dogs were enrolled prior to turning two and will be followed throughout their lives in all aspects: what they eat, what chemicals they encounter, what their health regimen entails, even where they sleep.

Why Golden Retrievers? For starters, between 30-to-60 percent of them get cancer. And according to the American Kennel Club they are the third most popular dog breed several years running, so there are a lot of them. They also have a wide range of roles, thus exposing them to a variety of environments, as pets, show dogs, therapy/assistance dogs, hunting dogs, competitors in different

events and search and rescue. Golden Retrievers are also easygoing, eager to please and enjoy the company of various species, especially people. And perhaps even because, as bestselling author and Golden Retriever devotee Dean Koontz acknowledges, “In spite of their size, they think they are lap dogs, and in spite of being dogs, they think they are also human.”

While its oldest participant to date is three years shy of the typical onset age of cancer of 10 years, the study has produced some interesting facts that will all be continuously reviewed as to their relevance throughout the remainder of the study and beyond. For example, a 2017 research article “Population Characteristics of Golden Retriever Lifetime Study Enrollees,” shows 578 of the 3,044 Golden Retrievers enrolled in the program have pet health insurance, 95 percent of the dogs were acquired from breeders, and 97 percent sleep in the owner’s house, with one in five sleeping with its owner. Sixty percent live in a suburban environment compared to urban at 10 percent. Forty percent swim at least once a week. Only six percent of the enrollees are exposed to secondhand smoke. Most are fed — 22 percent from plastic water or food bowls — a commercial diet (85 percent), while 8 percent are fed a diet that is at least partially raw. As for environmental issues, 99 percent of the enrollees got moderate to very active exercise, presumably some on the 37 percent of yards that receive insecticide or herbicide treatments; one in four Golden Retrievers also snack on grass.

Of the 3,044 dogs, 38 percent (1,154) were spayed/neutered. Neutered males were generally taller and heavier (24 inches at the withers and 71.6 pounds) than intact males (22.8/64.1), and the same was true for spayed females (22.44 inches at the withers/60.2 pounds) than intact females (21.25/54.6).

As the study progresses, it will investigate the importance of reproductive hormones and obesity, according to Melissa Simpson, the lead author of the article: “The value of long-term prospective studies in the advancement of human and veterinary health is difficult to understate; many important disease associations have arisen from those studies and they continue to inform treatment and prevention recommendations and public health policy. The need for similar data in companion animals is equally important and this study is designed to address some of the gaps in evidence-based recommendations for veterinary medicine.”

The potential for the usefulness of the information gleaned from the Morris Foundation study is tremendous. Since we’ve yet to cure cancer, we can never be too sure what evidence will deliver our eureka moment.

As the saying goes, cancer sucks. Even though it’s now seven years

since her passing, I still wish we would’ve decided to end Nade’s suffering sooner. But when your dog has cancer, it’s not like a horrible accident that makes the end-of-life decision obvious. Or that there’s a “Suffer-O-Meter” that clearly proves when “it’s time.” The decision is never easy. I know I had countless conversations with Nade and pleaded for her to tell me when she was ready. After one such talk, she did — a horrific vomiting episode prompted an emergency clinic visit and a call to my vet that evening. Before the vet came to the house the next afternoon, we took the short car ride to the lake for a dip, cuddled, gorged on people food and rewatched “All Dogs Go to Heaven.” And for the zillionth time in our 13 years together I told her I loved her. And that someday cancer would be gone for good. Since we all know dogs and humans are good at working together, I finally believe we’re well on our way. 



Rachel Brix, CPDT-KA, is a veteran high school English teacher who, inspired by her dog Percy, resigned to pursue a career with dogs. Rachel is a member of Association of Professional Dog Trainers, Pet Professional Guild, and has been teaching and training dogs for a combined 20 years. Her passion is rescue dogs, and she has managed two animal shelters. She actively advocates for all animals, from working on puppy mill legislation to pioneering the only city-wide wild animal circus ban in Arkansas. She also spearheaded the committee that built Carroll County, Arkansas’ first and only dog park. Rachel has been published in several issues of *Chronicle of the Dog* and was nominated for a 2017 Dog Writers Association of America award. She presented a Short at the APDT Conference in 2017 and returns with another Short for 2018. She’s happiest at home with her husband and six rescue animals.