

The San Francisco Bay Scottish Terrier Club,
Inc.

CANINE CANCER SEMINAR

Saturday, April 6, 2002
Radisson Hotel, Sacramento, CA

Ch. Sandreg's Highland Katrine "Kati"

One day in July of 2000 I came home from work and went around the back to the kennel where my dogs were waiting for after work hugs and loves. As I rounded the corner I was stopped short by the scene I was confronted with as I looked into the large outdoor kennel. The cement floor was covered with blood. It looked like a war had taken place. I panicked and wildly checked each one of my four dogs for injuries. I couldn't find anything out of the ordinary. None of my bitches were due to come into season, but that was the next thing I checked. I found that our 7 year old, almost 8 year old girl Kati had blood on her urethra. She had been spayed 6 months prior, so I knew it was something that needed to be checked. I made an appointment with our veterinarian for the next day.

She conducted a number of tests, some she did in-house, and others she sent to outside labs. Since all those tests came back negative, she did x-rays and ultrasounds. They showed no abnormalities. However, one of the outside lab tests did show a bacterial infection in the bladder. So Kati was treated for a bladder infection. She was treated with antibiotics for three months, and at times she seemed to be better, and then we'd see blood in the urine again. During this three month period there were times when I felt uncomfortable with the treatment, and I would read some vet med books on bladder infections. According to the treatment books we were using the correct protocol and the duration of the treatment could be up to six months.

In October of that year when she was still intermittently urinating blood, I asked my vet to open the bladder and see what was going on in there. It was taking too long to clear up. What she found was what I had dreaded, and per our agreement she closed Kati up, without doing anything. She told me she thought Kati might have a couple of months to live. The devastation I felt is unexplainable. Kati was the foundation bitch in my breeding program, she had whelped four beautiful litters, but most importantly she was my friend, and I loved her. I was told there was no cure, but we would make her as comfortable as possible until the end.

I couldn't believe it! No way was my Kati going to die at age 7 or 8! I started reading everything I could find on bladder cancer. One day I found an article written by Dr. Marcia Dawson. In this article she described a protocol of laser surgery and Piroxicam for the treatment of canine bladder cancer. I immediately went to my vet's office, it was 6:00 p.m. on a Friday night, and waved this article in her face. "We have to do this," I screamed. "Find someone who can do this!" She started calling right then and there at

6:00 p.m. on a Friday night. After several calls she found a vet in our area who had the laser and was willing to try the surgery. She had never performed that particular surgery before, but was willing to do everything she could to give Kati a chance. Three days later and one month after the original surgery, Kati was on the operating table for laser surgery. She was in surgery for close to four hours! Her bladder was almost totally filled with cancer.

Kati recovered in just two days! She seemed to be back to her old self – chasing birds and barking at everything that moved in or around “her” yard. She had no complications from the surgery and she was no longer urinating blood. Even though I had been told that there was no cure, that we had only bought her some time, I still had hope that my Kati would live a long, normal life.

Kati’s life did seem normal for the next nine months. She was on a very strict schedule of medications – antibiotics, piroxicam, meds to protect the lining of her intestines, vitamins, and other herbal supplements, and she had monthly ultrasounds to track her progress.

It was during this time that I started thinking about the fact that I was so ignorant about canine bladder cancer, and any other cancers for that matter. I should have been suspicious sooner than I was about Kati’s symptoms. How could I really be a good breeder if I didn’t have knowledge of things that could so seriously affect the dogs that I loved so much? I needed to get educated; we all needed to get educated. And who better to do this than the doctors and researchers who were working on these diseases. Thank you, Dr. Leach, Dr. Modiano, Dr. Knapp, Dr. Madewell, Dr. Dawson, Dr. Adams and Dr. Connelly for sharing your knowledge and expertise with us. We will all look to you to continue your research and teaching, and maybe someday we will be able to say that because of your hard work, diligence and dedication we no longer have to worry about our beloved friends being afflicted by, and dying from, cancers.

We had to have Kati put down on October 20, 2001, just a few weeks short of her 9th birthday. It was not the cancer that killed her, but her kidneys started to fail, and her body and spirit seemed to be very tired. Chasing birds, playing in the water, and barking at the dogs next door were not fun anymore. She died very quietly and peacefully surrounded by people who knew and loved her.

I am very grateful that I had two wonderful vets treating Kati, both willing to try new things, to learn, to research, and to refer if necessary. I will always be grateful for the loving care they gave to Kati.

Thank you all for coming today; I hope you leave with a renewed desire to continue learning all that you can so that we can someday be rid of the terrible diseases that take the lives of our beloved pets.

Elizabeth Wise

Elizabeth Wise, Chairperson
SFBSTC Canine Cancer Seminar

CANINE URINARY BLADDER CANCER

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IN**

What is transitional cell carcinoma (TCC)? TCC is the most common form of cancer that arises from the urinary bladder in dogs. It is a malignant tumor that invades into the bladder wall and has the potential to spread to other organs in the body.

Are all dogs at risk for developing bladder cancer? Any dog can develop bladder cancer. TCC usually occurs in older dogs (average age 11 years), is more common in female dogs (2:1 ratio of females to males), and is more common in certain breeds of dogs (Scottish Terriers, West Highland White Terriers, Shetland Sheepdogs, Beagles).

What clinical signs or "symptoms" do dogs with TCC have? The most common clinical sign or symptoms in dogs with TCC are hematuria (blood in the urine) and stranguria (straining to urinate). It is important to note that these same symptoms are also the most common findings in dogs with bladder infections. Bladder infections are much more common than bladder cancer.

How is bladder cancer diagnosed? A tissue biopsy is necessary to make a definitive diagnosis of TCC. Results of urinalysis, other urine tests, and finding of a mass in the bladder on examination all provide suspicion of TCC, but a tissue diagnosis is needed to be sure. Other types of growths or tumors can also occur in the bladder, and a biopsy is needed to know which type is present.

How can a tissue sample be obtained? At least 3 methods exist to obtain a tissue biopsy: (1) surgery, (2) cystoscopy - insertion of a fiberoptic scope into the bladder, and (3) catheter biopsy. Surgery provides the best tissue samples and most information about the cancer in the bladder and other places in the abdomen. Surgery is also the most invasive of the 3 methods. For this reason, cystoscopy and catheter biopsies are often attempted first. There are some cases, however, where surgical biopsies become necessary to make the final diagnosis.

What other tests should be done to evaluate a dog with TCC? A CBC, serum biochemistry profile and urinalysis can help assess the dog's overall health. Urine culture is indicated if a secondary bacterial infection is suspected.

Tumor staging (tests conducted to determine if/where the tumor has spread) is accomplished with radiographs (x-rays) of the thorax and abdomen and abdominal ultrasound. To visualize the tumor in the bladder, contrast cystography ("x-rays" made while a "dye" is in the bladder) and ultrasound made while the bladder is full with fluid (urine or sterile saline) are performed. Spread of the TCC beyond the urinary tract is discovered in approximately 20% of dogs at the time of diagnosis. Kidney dysfunction can occur due to urinary tract obstruction and secondary bacterial infection (which is common in dogs with TCC).

How is TCC treated in dogs? Surgical excision of TCC is usually not possible. This is because the tumor is often located in the neck or trigone area of the bladder and has spread down the urethra in many cases. In the trigone area of the bladder, the ureters (tubes that connect the kidneys to the bladder) and urethra (tube that leads from the bladder to the outside) join the bladder. Also, muscles in the part of the urethra near the bladder control when the dog urinates. Since these structures are vital, it is not possible to remove this area of the bladder. In addition, if the TCC has spread beyond the urinary tract, then successful tumor removal is even less likely. One question that has not been answered to date is this: does removal of part of the tumor (surgical debulking) aid in treatment? We are currently reviewing the records of 122 dogs that had various types of surgical intervention to answer this question.

Radiation therapy has been used in a small number of dogs with TCC. Although the TCC growth was controlled in these dogs, side effects of the therapy included fibrosis (thickening and hardening of the bladder) and incontinence. These side effects were not considered acceptable. It is possible that different radiation protocols may be effective in the future.

The results of chemotherapy for canine TCC have been disappointing. Drugs tested to date have induced remission in <20% of dogs when given as a single agent. Combination therapy protocols may be more effective, but information on these in dogs is lacking. On one positive note, it is worth pointing out that dogs, in general, tolerate chemotherapy better than humans. The chemotherapy protocols that we used most often result in a good quality of life for 90% or more of the treatment period.

A type of medical therapy for TCC that has shown promise is cyclooxygenase (cox) inhibitor treatment. Cox inhibitors, also called nonsteroidal antiinflammatory drugs, include aspirin, ibuprofen, and piroxicam. Piroxicam (Feldene, Pfizer, Inc.) has received the most attention of these drugs. Piroxicam, given to 62 dogs with TCC at a dosage of 0.3 mg/kg, orally, once daily, resulted in complete remission in 2 dogs, partial remission ($\geq 50\%$

tumor shrink) in 9 dogs, stable disease (<50% change in tumor volume) in 35 dogs, and progressive disease in 16 dogs. The median survival was 195 days with 20% of dogs living a year or more. Piroxicam works differently than chemotherapy. Piroxicam induces apoptosis (programmed cancer cell death), and may also have an effect on the tumor blood supply. Most dogs treated with piroxicam have excellent quality of life. Piroxicam helps control pain associated with the tumor and pain from concurrent conditions, such as arthritis.

In an attempt to improve the efficacy of therapy, piroxicam is being combined with chemotherapy in clinical trials. We first attempted to combine piroxicam with the chemotherapeutic agent cisplatin. The antitumor effects of this combination were very impressive (remission in 10 of 14 dogs), BUT, this treatment was toxic to the kidneys. We do not currently recommend use of this combination. We are conducting clinical studies to determine ways to limit the kidney toxicity of this therapy while maintaining the antitumor activity. We have also conducted a study of carboplatin chemotherapy combined with piroxicam. This combination did not have kidney toxicity, and appeared more effective than piroxicam alone or carboplatin alone. Preliminary results include a remission rate of 40%. Because carboplatin is eliminated from the body through the kidneys, careful evaluation of the kidneys (through blood tests, urinalysis, and ultrasonography) are recommended before selecting the dose of carboplatin to be used. The Veterinary Cooperative Oncology Group is conducting a study of mitoxantrone chemotherapy combined with piroxicam, and preliminary results suggest this combination will be similar in efficacy to carboplatin/piroxicam.

What is the prognosis for dogs with TCC? The "good news" is that TCC can be controlled for a period of time in many dogs. The "bad news" is that most dogs with TCC are not currently cured. Median survival for dogs treated with single agent chemotherapy in our studies was 130 days. Median survival for 62 dogs treated with piroxicam alone was 195 days. Median survival for dogs treated with cisplatin combined with piroxicam was 250 days (but due to kidney toxicity, we do not recommend this protocol). Survival times for dogs being treated with other chemotherapeutic agents combined with piroxicam are currently being studied.

How can we improve the outlook for dogs with TCC? Our group, the Purdue Comparative Oncology Program, is conducting investigations in several areas to answer this question. We need to answer the questions: (1) how can TCC be prevented, (2) how can TCC be diagnosed earlier, and (3) how can existing TCC be treated more effectively?

How can TCC be prevented? In order to prevent TCC, we must determine what causes TCC. TCC, like most cancers, is thought to develop through a combination of environmental and genetic factors. To determine what the environmental factors are, we are conducting a case control study in Scottish Terriers in which we compare the exposure to certain factors in dogs with TCC compared to those factors in dogs without TCC. In a similar study conducted several years ago, Dr. Larry Glickman found that exposure to insecticides and obesity were risk factors for TCC occurrence. The insecticides included flea dips. Since the types of insecticide in use today are different than those used several years ago, we are now looking for the effects of these newer generation insecticides. We will also study the effects of second-hand cigarette smoke, dietary factors and others.

To determine what genetic factors are involved in TCC development, we are working with Dr. Fred Leach at the National Cancer Institute. Dr. Leach is studying DNA changes in dogs with TCC (compared to the DNA of dogs without TCC). His work will benefit dogs, and will help identify genetic changes that will also be investigated in human TCC patients.

How can TCC be diagnosed earlier? If TCC could be diagnosed earlier, then the treatment may be more successful. Attempts to diagnose TCC earlier have included the development of urine tests to detect tumor antigens shed from the tumor cells. Examples of these tests include Bard test and BTA test. These tests have been found to have high sensitivity for TCC, but low specificity. In other words, if a urine antigen test is negative, it is very unlikely that the dog has TCC. But, if the test is positive, it does not necessarily mean that the dog has TCC. A positive test can be the result of blood in the urine from any cause, infection, inflammation, or cancer. One of the goals we have with information we are obtaining from the case control study and from evaluation of a different urine test, is to determine the best way to screen older, yet still clinically "normal" Scotties for the presence of early stage bladder cancer.

What can be done to improve the therapy for existing TCC? Investigations to answer this question fall into 2 categories: (1) research to make the best use of the medications we already have access to, and (2) research to develop better, new drugs. The first part of this research includes studies to determine which combination of chemotherapeutic agents with and without piroxicam or piroxicam-like drugs has the most efficacy against TCC. Studies to further determine the role of surgery or radiation therapy are also needed.

The second part of this research is to find new targets for cancer therapy. Most traditional chemotherapeutic agents kill cancer cells by interfering with

DNA replication and with cell division. These drugs, however, do not selectively kill cancer cells, they damage normal cells as well. In addition, cancer cells have evolved to the point of having many different growth pathways to allow them to continue to grow even in the face of chemotherapy. The cancer will continue to progress in many cases. The damage to normal cells results in toxicity and side effects. Therefore, many laboratories, including our lab are working to identify new targets in the cancer cells that are not present or not needed by normal cells. Drugs which "hit" these targets have the potential to be much more effective and less toxic than our current chemotherapeutics. We are working with laboratories at Purdue University and at Harvard University on two potential new targets for bladder cancer therapy.

How can dogs with TCC help people with TCC? Certain forms of naturally occurring cancer that strike our pet dogs, are very similar to those same forms of cancer in humans. This is not true for all canine cancers, but this is true for invasive urinary bladder cancer. TCC in dogs is virtually identical to high grade muscle invasive TCC in humans. [Please note that humans also get a lower grade, superficial TCC that is very different than the high-grade invasive disease. Dogs rarely get this less aggressive, low-grade form of TCC]. Canine TCC and human invasive TCC are very similar in histopathologic characteristics, cellular and molecular features, biologic behavior, prognostic factors, and response to therapy. Information learned from dogs with TCC, can help provide new information to better understand and treat human TCC.

We are very pleased to be involved in two collaborative studies being conducted at Indiana University. These studies involve clinical trials of cox inhibitors in people with high-grade bladder cancer. In the first study, 2 of the first 4 patients enrolled have had complete remission of their cancer - and this is after they had failed to respond to "standard treatment"! The second clinical trial is just getting underway. It is thrilling to be involved in work that is of benefit to both pet animals and people.

What can you do to help in making progress in TCC?

Case control study. We need your help with ongoing studies. The Scottish Terrier Club of America and the American Kennel Club Canine Health Foundation are funding a case control study to identify the risk factors and protective factors for TCC development. Pet owners of Scottish Terriers with TCC and owners of Scottish Terriers without TCC are asked to fill in a questionnaire describing their dog's medical history and exposure to potential risk factors (diet, drugs, cigarette smoke, pesticides, etc.). We will then compare the exposures of these various factors in dogs with TCC compared to dogs that did not develop TCC. This will allow us to identify

which factors put dogs at risk for TCC, and which factors may protect a dog from developing TCC. We have an excellent start on this project, to date, with information collected from 66 TCC cases and 66 control dogs. For this case control study, we would like to collect information from an additional 34 Scottish Terriers that have had TCC diagnosed anytime during or after 1995. We also need information from 34 more Scottish Terriers who do not have TCC (who reached 6 years of age or older in the study period of 1995-2002).

We need to receive completed questionnaires by May 15, 2002. To participate in this study, you may contact: Dr. Marcia Dawson by email at: dmdawson@voyager.net, or Ms. Patty Bonney at Purdue University, (765) 494-1130.

Genetic evaluation. We are working with Dr. Fred Leach at the National Cancer Institute to determine the genetic factors involved in TCC development. Pet owners that have dogs with TCC can help in these efforts by allowing their veterinarian to collect and send a blood sample to Dr. Fred Leach. If dogs with TCC have tumor tissue collected (at time of biopsy, surgery, or autopsy/necropsy), then sending a tissue sample to Dr. Leach will be very helpful. Dr. Leach can be contacted at: National Cancer Institute, 10 Center Dr, Building 10, Room 2B47, Bethesda, MD 20892-1501 or by email at leach@mail.nih.gov.

Clinical trials. An important way to make progress against TCC is to conduct clinical trials. At Purdue University, we currently have three clinical trials in progress, one is a treatment trial to determine how to safely combine chemotherapy and cox inhibitors while maintaining antitumor activity. A second trial is to evaluate a protocol that is aimed at controlling the tumor's blood supply (the cancer cannot grow without a growing blood supply), and the third is a study being done on tissue samples collected at the time of euthanasia (when the pet owner has determined that quality of life has deteriorated and euthanasia is the most humane action at that point). This study involves instillation of a new type of medication into the bladder and collection of bladder tissues at necropsy (autopsy). This study is crucial in the development of a promising new target treatment.

Other oncologists also have ongoing clinical trials for TCC. And, more clinical trials are needed - most dogs with TCC do not enter clinical trials. If you have a dog with TCC, speak to your veterinarian about any clinical trials being done in your area of the country. Some of the work being done at Purdue University is summarized on our website <http://www.vet.purdue.edu/vcs/Pcop/Homepage.html>.

The Veterinary Cancer Society website also provides information on studies around the country (www.vetcancersociety.org).

Support for investigation and for programs that contribute to the fight against TCC. Donation of money to help support programs and research is always helpful. Many people do not realize how limited funding for investigative work is. Much of the important medical research being performed in this country is being done at colleges and universities. Yet, many "state supported" universities (such as Purdue University) receive less than 20% of their operating budget from their state. The remaining funds must be obtained from gifts and from research grants. Support goes beyond funding. Important support can include educational programs such as this one.

References:

Knapp, DW. Tumors of the urinary system. In: Small Animal Clinical Oncology, 3rd Ed. SJ Withrow, EG MacEwen, eds. WB Saunders, Philadelphia, 2001, pp490-499.

Knapp, DW, Waters, DJ, Schmidt BR. Tumors of the urogenital system and mammary glands. In: SJ Ettinger, EC Feldman eds. Textbook of Veterinary Internal Medicine, 5th Ed. WB Saunders, Philadelphia, 2000, pp 541-546.

Knapp, DW, Glickman NW, DeNicola DB, et al. Naturally-occurring canine transitional cell carcinoma of the urinary bladder. A relevant model of human invasive bladder cancer. Urolog Oncol 5:47-59, 2000.

Knapp DW, Glickman, NW, Widmer WR, et al. Cisplatin versus cisplatin combined with piroxicam in a canine model of human invasive urinary bladder cancer. Cancer Chemother Pharmacol 46:221-225, 2000.

Mohammed SI, Bennett PF, Craig BF, Knapp, DW. Effects of the cyclooxygenase inhibitor, piroxicam, on tumor response, apoptosis, and angiogenesis in a canine model of human invasive urinary bladder cancer. Cancer Res 62:356-358, 2002.

**WHERE DO WE GO FROM HERE?
Bladder Cancer Update
(taken from *The Bagpiper*/2000 Number Two)**

Marcia Dawson, DVM

Another Scottie with bladder cancer. It is getting to be an all too familiar and sad story. This time the Scottie lived in New England, but it doesn't seem to matter where they live. The South, the Midwest, the Southwest, or Northwest. We have bladder cancer diagnosed in Scotties as young as 7 years of age all the way to 12 and 13. We have males and females, neutered and intact, champions with royal blood and rescued pets. In the past few months there has been a wave of response from Scottie owners all over the country, writing me to tell the same gut wrenching stories. Take heed, my fellow Scottie owners and friends: we have a big problem.

Several people have asked me what is new, what is being done, what can they do to help? News of a new bladder cancer test, rumors of new treatments and a possible cancer survey have everyone's interest fired up. Some answers are in order.

A REVIEW OF WHAT WE KNOW

Dr. Deborah Knapp, the well-known oncologist and bladder cancer expert at Purdue University, recently published a paper in *The Journal of Urologic Oncology* entitled "Naturally Occurring canine transitional cell carcinoma of the urinary bladder-A relevant model of human invasive bladder cancer". The stated purpose of Dr. Knapp's paper is to characterize spontaneous invasive transitional cell carcinoma (TCC) of the bladder in dogs, to summarize, compare, and contrast the canine disease with the human version, and assess the suitability of the dog as a model for human research. This paper summarizes well what we do know about TCC in dogs in general and has important implications for Scotties as well. (All data listed below is for the general dog population unless otherwise stated.)

Frequency-TCC is the most common urinary tract cancer in the general dog population at 1.5-2% of all cancers. As more and more cancer is diagnosed in dogs, this seemingly low percentage actually represents a sizable number of patients diagnosed yearly with TCC. We do not know the true prevalence of this disease in Scotties.

The average age at the time of diagnosis is 10 years.

The most common clinical signs of TCC are bloody urine, straining to urinate, and recurrent urinary tract infections, which do not clear up with antibiotics.

20% of the patients already have metastatic disease at the time of diagnosis. The most common sites of metastasis are the regional (nearby) lymph nodes and lungs.

Females are over-represented 2:1. There is an increased risk for neutered dogs of either gender.

The tumor is nearly always located in the trigone or neck of the bladder, a site not conducive to successful surgical excision by traditional methods. Radiation therapy carries a great risk for adverse side effects and is not used routinely.

Chemotherapeutic options are currently limited and not very effective. Dr. Knapp has mentioned a combination therapy of piroxicam and cisplatin, which is remarkably effective in reducing tumor size, but has been too toxic to the kidneys for recommended use at this time. For now, piroxicam remains the treatment of choice with more therapies being tested and explored.

Some Scottie owners have tried various alternative therapies including Vitamin C and E, shark cartilage, garlic, omega-3 fatty acids, milk thistle, and Co-Enzyme Q, but to my knowledge, no clinical trials have been run to test the benefit of these treatments.

KNOWN RISK FACTORS

Dr. Knapp reiterates known risk factors for bladder cancer, some of which were identified by Dr. Larry Glickman in a paper entitled "Epidemiologic Study of Insecticide Exposures, Obesity, and Risk of Bladder Cancer in Household Dogs", published in 1989 *The Journal of Toxicology and Environmental Health*. These include:

Exposure to topical insecticides used for flea and tick control including dips, sprays, and powders. These products consist of a variety of active ingredients, synergistic compounds, and inert ingredients, which are the petroleum distillates and solvents used to disperse the active compounds over and through the skin. (These insecticides did not include the newer generation flea control products such as Advantage, Frontline, Sentinel, and Revolution, which were not on the market at

the time of this study).

Obesity: higher risk due to the concentration of toxic compounds in body fat;

Proximity to a marsh or swamp that had been routinely treated for mosquito control;

And most shocking of all, an identified breed risk for bladder cancer: Scottish Terriers are as much as **18 times more likely to develop TCC than mixed breeds and other purebred dogs**. No other breed comes close to the risk or odds ratio of the Scottie for developing this cancer.

Dr. Knapp writes, "The cause of the breed associated risk is not known, but in all likelihood, it represents predisposition to bladder cancer in metabolic activation and detoxification pathways."

Don't these words just leap off the page? What Dr. Knapp is suggesting here is that our dogs have something different about them, something unique in their genetic makeup that permits the activation of precancerous cells, overrides the normal defense mechanisms to remove these dangerous cells, and allows the process of oncogenesis, or birth of cancer, to go unchecked. And did you notice the words "detoxification pathways"? That is scientific code for LIVER. Dr. Knapp suspects a connection between cancer and the Scottie liver's inability to adequately detoxify carcinogens or other poisons, which then come in contact with the lining of the bladder during excretion. Could there be a connection between the liver problems so many of us are seeing in our Scotties and this high rate of TCC and other cancers? You bet.

WHAT IS NEW

There has been a lot of talk recently about a new bladder cancer test now available through your veterinarian. This test, marketed by Abbot Labs, is called the Veterinary Bladder Tumor Analytes, or V-BTA, test and is a urine dipstick assay which measures a tumor protein complex detectable in the urine of dogs with TCC. The V-BTA has a high sensitivity and good negative predictive value, which makes it useful to help rule out bladder cancer in a dog experiencing symptoms. If the test comes up negative, then TCC may not be the problem. Unfortunately, the test does not have a high specificity for TCC, and false positives may be common since the test will react with other

components in the urine to give the wrong result. Therefore, if the test comes up positive, more diagnostic work is called for, such as ultrasound or cystoscopy, to rule out or find a tumor. In fact, even if there were a negative V-BTA test, I would still recommend a complete work up in an older dog straining to urinate and passing bloody urine. In other words, you cannot rely on this test alone. While the V-BTA test is not foolproof, it is the first of its kind and may have a place in diagnostic workups for TCC in Scotties.

In another interesting development, I have been in contact with a Scottie owner in New York whose 9-year-old spayed female was diagnosed with TCC in early December of 1999. The disease was advanced, as usual, and the treatment options consisted of doing nothing, piroxicam only, more advanced chemotherapy, and surgery, which was discouraged by her veterinarian. Stormy was given 3 months to live. But this owner was persistent and demanded another opinion. The referral surgeon suggested that excision be performed using a high tech diode CO2 laser borrowed from a colleague, a procedure he had not done before but which gave Stormy her best chances. The surgery was performed the 16th of December and the surgeon's report was very optimistic. He believed that he had removed all traces of tumor from the bladder wall, and the histopathology report on submitted tissue supported his claim. As of March 16, 2000, Stormy is disease free, feeling well, and has no signs of recurrence. Her veterinarian will be using the V-BTA test routinely to check for regrowth, and in the meantime, Stormy is beating the odds. Although laser surgery is not readily available in all veterinary practices, eventually lasers will be used more routinely, and surgeries like Stormy's will become much more commonplace and affordable.

And finally, what about that Scottie survey-is it a reality? Not yet, but hopefully in the near future. One possible design is a longevity, morbidity, and mortality survey of our breed. This kind of survey can provide a huge amount of valuable information for us all and serve as a tremendously important database for future research plans, not just for Scotties and other dogs, but for humans as well. With a valid survey, we can get down to basics and find out what is sickening and killing our dogs. What is the actual prevalence of bladder and other cancers and liver disease in Scotties? What is the lifetime risk for the different cancers in our breed? Are their risk factors specific to Scotties, which set them apart from the general population? Is there significant correlation between high cancer rates in Scotties and their environment, life style, insecticide/drug use, food and water

consumption, and yes, their pedigree? By identifying risk factors specific to Scotties, would we not be taking a huge step toward *preventing* TCC?

The results of a survey such as this could be a springboard for some very tantalizing research possibilities:

Collaborative research with other institutions such as the National Cancer Institute to identify genes that put specific dogs like Scotties at risk for TCC;

Studies to develop new reliable markers in the urine of affected dogs; a test that would go beyond the V-BTA to absolutely diagnose or rule out TCC - a test that could be used as a screening test for diagnosing TCC much earlier in the course of the disease before metastasis takes place;

Liver enzyme studies to define certain enzymatic pathways in the liver and to develop tests that may predict defects in drugs and carcinogen metabolism.

I am breathless with excitement over the possibilities. We all know how special our Scotties are, but there really is something very unique about them with respect to cancer that may have far-reaching benefits beyond our wildest hopes and imaginations. Where do we go from here? We get down to work!

References

Knapp, D., Glickman, M., DeNicola, D., Bonney, P., Lin, T., and Glickman, L.: Naturally occurring canine transitional cell carcinoma of the urinary bladder: a relevant model of human invasive bladder cancer. *J. Urologic Oncology*, 5:47-59, 2000

Glickman, L., Schofer, F., McKee, L.: Epidemiologic study of insecticide exposures, obesity, and risk of bladder cancer in household dogs. *J. Toxicology and Environmental Health*. 28:407-414, 1989.