# Bladder Cancer Study- Final Report

***What Every Scottie Owner Needs To Know***

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If you have never lost a Scottish Terrier to bladder cancer – or, more properly, Transitional Cell Carcinoma – consider yourself extremely lucky. Scotties have an 18 times greater likelihood of contracting the disease than their mixed-breed counterparts.

TCC is a growing concern. In North American veterinary teaching hospitals, the prevalence of dogs diagnosed with the disease has increased by more than 600% between l975 and 1995! Several breeds are at a significantly increased risk of developing TCC, including Shetland Sheepdogs, Wire Fox Terriers and Westies, but none quite as dramatic as the increase in risk associated with Scottish Terriers. This dramatic increase in TCC risk suggests a genetic predisposition to TCC in terriers and primarily in Scottish Terriers.[1]

In June 2001, the first scientific study of Transitional Cell Carcinoma (TCC) in Scotties was undertaken. Thanks to matching funds from the Scottish Terrier Club of America's Health Trust Fund and the AKC Canine Health Foundation, a Purdue University research team orchestrated AKC CHF Grant No 2105: *Characterization of Host and Environmental Risk Factors for Urinary Bladder Cancer in a High Risk Breed (The Scottish Terrier).*

It is believed that TCC in dogs is probably multi-factorial involving both a genetic predisposition for the development of the cancer as well as environmental triggers that may "turn on" the process in susceptible individuals. Prior epidemiologic research[2] conducted in a wide variety of dogs already identified certain risk factors for TCC. In this case/control study conducted in 1989, the risk of TCC was found to be unrelated to second hand cigarette smoke and household chemical exposures, but the risk was significantly increased for dogs exposed to topical insecticides, particularly the older generation flea and tick dips. If the dogs were obese or even moderately overweight, the increased risk was enhanced. Furthermore, if the dogs lived near a marsh, or any environment that could be another potential source of insecticides, the risk for TCC was enhanced.

In 1991, the National Institutes of Health (NIH) published its findings of a case/control study which reported an increased risk for malignant lymphoma in pet dogs exposed to the commonly used lawn and garden phenoxy class of herbicide, 2,4-D.[3] In this study involving over 1000 dogs, there was a greater than 2 fold increased risk of lymphoma in dogs exposed to lawns, treated either by the home owner or by a commercial company, four or more times per year. Although these findings were challenged[4] and later refuted[5] by a Chemical Industry Task Force , a subsequent study[6] demonstrated that dogs exposed to lawns treated with 2,4-D absorb enough of the chemical to excrete it in the urine for several days after the herbicide treatment.

With this earlier research as a starting point, the Purdue researchers now decided to test three specific hypotheses:
1) That exposure to lawn and garden chemicals will increase the risk for TCC in Scottish Terriers;
2) That exposure to flea and tick products will increase the risk for TCC in Scotties:
3) That certain foods, in particular certain vegetables and vitamin supplements, fed on a routine basis, will reduce the risk for TCC in Scotties.

Scottie owners were recruited via the STCA and Purdue Comparative Oncology Program websites. Many STCA members were personally contacted by veterinarian and Scottie breeder Marcia Dawson, who served on the research team, along with Lawrence Glickman, VMD, DrPH, Malathi Raghavan, DVM, PhD, Deborah Knapp, DVM, MS, DACVIM and Patty Bonney, RVT from the Purdue School of Veterinary Medicine.

Potential participants received a lengthy – 15 page – questionnaire, asking a multitude of questions on diet, supplements, medications, use of flea and tick preparations, general husbandry, and exposure to lawn and garden chemicals. None of the participants were aware of the hypotheses being tested in the study. In order to be eligible, a Scottie had to be diagnosed with TCC after January 1, 1995, and the owner had to submit proof of diagnosis. Dogs diagnosed via biopsy were considered "confirmed" and dogs diagnosed via cytology (needle aspiration, urinalysis, etc.) were considered "presumptive." Control dogs – those who would provide comparison information so that scientific conclusions could be reached – were limited to Scotties who had never been diagnosed with TCC and were at least six years old on or after July 1995. Dogs with a recent history of urinary tract disease were eliminated from further study. Only one dog per household could participate.

Demographic information was collected on the 83 case (diagnosed with TCC) and 83 control dogs. It was found that, at the time of data collection, 63% of the diagnosed dogs had died, compared with only 12% of controls. Both groups were similar in age, with case dogs averaging 9.9 years, and controls, 9.1. Forty-one percent in both groups were males, and 59% were females. Most were neutered – not surprising, given their relatively advanced ages.

Data were subjected to rigorous statistical analysis and the conclusions drawn are troubling indeed. **Scotties who had been exposed to lawn herbicides were between four and seven times more likely to develop bladder cancer than dogs that had not been exposed.**

Fifty-one percent of the diagnosed dogs had been exposed to herbicides on more than an occasional basis, compared to 18% of controls. The number of case and control dogs exposed to insecticides was equal, thereby suggesting that – in this study - exposure to insecticides **alone** does not appear to be a significant risk factor. However, exposure to herbicides alone resulted in a nearly four times greater risk of developing bladder cancer, and exposure to both insecticides and herbicides increased the likelihood to over seven times! In other words, a Scottie exposed to herbicides on a more-than-sporadic basis is

four times more likely to be diagnosed with bladder cancer, and the odds skyrocket to **seven times more likely when herbicides and insecticides are combined.**

The risk appeared to be greater for lawn products containing a common chemical known as 2,4-D, which is a phenoxy herbicide. Data suggest that non-phenoxy herbicides also increase the cancer risk, but results were not statistically significant. Researchers concluded that the data are consistent with a genetic-environmental interaction, meaning that Scotties with a genetic predisposition are at high risk for TCC when exposed to certain risk factors like phenoxy herbicides.

The report warns that the inert ingredients in herbicides may also be responsible. The inert ingredients – which can comprise more than half of the preparation by volume – need not be listed on the label, but often include hazardous and carcinogenic chemicals. The authors urge Scottie owners to significantly reduce access to treated lawns when either phenoxy or non-phenoxy products are used. They also recommend that Scottie owners get semi-annual microscopic examination of their pet's urine, so that TCC can be detected in its early – and potentially treatable – stages.[7]

Testing the second hypothesis, the researchers looked at the relationship between use of topical flea and tick products and increased incidence of TCC. Those Scotties whose owners indicated that they had a history of exposure to such products were included in the study. Eighty-eight dogs diagnosed with TCC made up the case group, with 83 Scotties serving as controls. Owners had to have used fleas and tick products within one year prior to diagnosis in the TCC dogs, and a comparable period of time for controls. In dogs that had died prior to the study, the specified products had to have been used within one year prior to the dog's death. Products under study included shampoos, dips, collars, powders, sprays, pills and "spot-ons" – the products that are "dribbled" down the dog's back. Owners were asked to provide brand names, and – to ensure the validity of the data – to provide labels as well.

Interestingly – and sadly – the most common health problem confronting the control dogs at the time of data collection was cancer, which affected 24% of the non-TCC dogs. Also significant is the fact that only 5% of control dogs had a history of urinary tract disease prior to the study, whereas 28% of the TCC dogs had chronic problems.

Risk factors found to be significantly associated with increased risk for TCC included age, weight, having been neutered, having a close relative with a history of TCC, and, oddly enough, black coat color, although there may be some confounding factors to explain this. Exposure to the older class of flea and tick products such as powders, dips, and collars resulted in an increased risk of TCC. Using multiple products and using them more frequently also increased the risk. The relationship between use of "old-fashioned" flea/tick products and TCC was increased for overweight dogs, again suggesting that toxins stored in fat cells pose more risk due to longer exposure. The good news is that the use of "spot-ons" (Frontline ® and Advantage®) – which represent the new generation of product designed for the war on external parasites – did not result in any increased risk for bladder cancer.

Researchers advise Scottie owners to avoid the older topical flea and tick products, specifically dips, powders and collars, and to use the newer spot-on products, particularly those containing fipronil (Frontline®).[8]

In the third study, 93 Cases and 83 Controls were studied to assess the effects of vegetable consumption and vitamin A, C and E supplementation on the risk for TCC. Research on humans suggests that the risk of certain kinds of cancer is reduced by as much as 60% when vegetables are a significant part of the diet. However, the connection to bladder cancer is not clear, and no study before has looked at vegetable consumption and cancer risk in dogs.

Owners were asked to provide detailed information on diet, and, as any nutritionist would predict, vegetable consumption correlated negatively with bladder cancer risk in Scottish Terriers.[9] Type of vegetable made a difference, with positive effects seen in dogs fed either leafy green or yellow-orange vegetables. Cruciferous vegetables such as broccoli had a protective effect, but the sample size in this study was too small to be significant. Also, no difference between Cases and Controls was found if veggies were fed only once a week or less; in order to have a positive effect, vegetables had to be fed at least three times per week. Scotties fed either leafy green or yellow-orange vegetables at least three times a week were 70% to 90% less likely to develop bladder cancer than their cohorts! Over half of the dogs studied were fed vegetables at least once a week, with carrots being the most popular choice. None of the vitamin supplements showed a significant decrease in risk.[9]

Over 50,000 men and women are diagnosed with bladder cancer each year. Animal studies on risk factors, to which our breed has made a significant contribution, may teach researchers more about how humans contract the disease. Furthermore, this important study will serve as a springboard for future research. For example, Dr. Glickman and his team currently have a study underway looking at the concentration of potentially dangerous chemicals in the urine of children and their pet dog(s) exposed to herbicide treated lawns. Future studies may include prospective trials using vegetables to prevent TCC in our Scotties. The Purdue study will not only make our Scotties' lives better, but the results may also someday help make human lives better as well.

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