

Fall / Winter 2018

Questions? Comments?
Suggestions?

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IN THIS ISSUE

- 3** On the Health Front
- 4** Digestive System
Inflammatory Bowel
Disease (IBD)
- 10** Westie Owners Launch
GoFundMe Page, Raise
Funds for Innovative IPF
Study
- 13** Studying Cancer in Dogs
as a Path Towards a World
Where We No Longer Fear
Cancer - A Contemporary
Update on Canine
Hemangiosarcoma
- 15** Canine Transitional
Cell Carcinoma (TCC)
/ Urothelial Carcinoma
(UC) / Bladder Cancer
in Dogs - New research
provides an opportunity
for early detection in the
West Highland White
Terrier
- 19** Let the IRS Help

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PRESIDENT'S MESSAGE

The WFA continues to be very grateful for its exemplary Board of Directors and Advisory Council. At the Annual Board meeting on October 4, 2018, in Exton, PA, the board elected Randy Cantrell and Dean Nelson to the Board of Directors and honored Fred Askin, MD with his election to the Advisory Council. Mr. Cantrell is a coach in executive/CEO leadership and Mr. Nelson is a Certified Public Accountant (retired). Dr. Askin is a pathologist at John Hopkins Hospital and professor of pathology at the John Hopkins University School of Medicine. We thank these gentlemen for volunteering to serve and share their knowledge and experience.



Bebe Pinter

In this issue start reading about the Digestive System's Inflammatory Bowel Disease (IBD) from our **The Westie Health Book**. Subtopics include: How does a dog develop IBD? What are the clinical signs of IBD? How is IBD diagnosed? and Treatment of IBD. Dietary changes are one of the most important components of treatment.

Teresa Barnes, vice president communications, provides an in depth view of grassroots fundraising with her article "*Westie Owners Launch GoFundme Page, Raise Funds for Innovative IPF Study*". On behalf of the board of directors, we sincerely thank PJ Kessler and the team for taking an active role.

Thank you to Drs. Borgatti, Fahrenkrug, and Modiano, Animal Cancer Care and Research Program, University of Minnesota for their report "*Studying Cancer in Dogs as a Path Towards a World Where We No Longer Fear Cancer—A Contemporary Update on Canine Hemangiosarcoma*". According to their report, Hemangiosarcoma is most common in dogs and research shows promising results in regards to treatments and early detection.

The next article is "*Canine Transitional Cell Carcinoma (TCC) /Urothelial Carcinoma (UC) bladder cancer in dogs—New research provides an opportunity*

(Continued on page 2)

(President's Message continued from page 1)

for early detection in the West Highland White Terrier” by Drs. Matthew Breen and Shelly Vaden, North Carolina State University College of Veterinary Medicine. According to the authors this cancer is the most common of the canine urinary tract and occurs in about 1-2% of all canines. Early detection is key to helping our Westies.

The final article “Let the IRS Help” is contributed by Tom Barrie, WFA director. Mr. Barrie provides numerous effective and tax-efficient ways beneficial to donors in supporting Westie health research through the WFA.

We need your help and encourage you to support our mission by becoming an annual WFA donor. We are an active board for a canine foundation that is making real progress to improve health in the West Highland White Terrier breed. You may contact Jim McCain, Donor Manager at donormanager@westiefoundation.org or visit our website www.westiefoundation.org for assistance. In addition, I would be delighted to visit with you about what the WFA has accomplished and major projects and research underway.

Thank you for your continued involvement and support of the WFA but most of all, your love of Westies!

Bebe Pinter



The Westie Foundation of America, Inc is a nonprofit corporation, recognized by the IRS as a 501 (C) (3) organization. The mission of the Foundation is to advance and support medical research to benefit the health and quality of life of West Highland White Terriers: and to further develop and communicate information regarding the health, care, breeding and quality of life of Westies to Westie owners, Westie breeders and veterinarians.



Request for Samples

RESEARCH PROJECT	SAMPLES NEEDED	CONTACT INFORMATION
Genetic marker for Atopic Dermatitis	Saliva swabs or blood samples from dogs with skin disease or from normal dogs 5 years of age or older from family lines free of allergies	Kim Williams North Carolina State University 919-513-7235 kdwilli4@ncsu.edu
Genetic susceptibility of Transitional Cell Carcinoma (TCC) (Bladder Cancer)	Blood samples from dogs diagnosed with TCC and dogs over the age of nine who have no known cancers	Gretchen Carpintero Ostrander Lab National Human Genome Research Institute 301-451-9390 Dog_genome@mail.nih.gov
Genetic marker for Addison's Disease	DNA from cheek cells and/or blood from affected dogs and unaffected dogs over the age of 7	Dr. A.M. Oberbauer UC Veterinary School (Davis) 530-752-4997 http://cgap.ucdavis.edu/
Clinical Features and Genetic Basis of Idiopathic Pulmonary Fibrosis (IPF)	Blood samples from dogs diagnosed with PF and healthy dogs over age 8 without lung disease	Drs. Ned Patterson and Peter Bitterman Katie Minor (contact) University of Minnesota 612-624-5322 minork@umn.edu
Idiopathic Pulmonary Fibrosis (IPF)	Cheek and/or blood samples from dogs diagnosed with pulmonary fibrosis	Dr. Victor J. Thannickal University of Alabama Sample collection coordinated by Dr. Pamela Whiting, DVM pgwhitingdvm@aol.com 707-529-9222 (cell/text) 707-837-8101 (clinic)
Dry Eye Syndrome (keratoconjunctivitis sicca)	Dogs diagnosed with dry eye and dogs over 7 years old with no ocular abnormalities *participants must be available for appointments at UC Davis Veterinary Center (CA)	Dr. Sara Thomasy UC Veterinary School (Davis) 530-752-1770 smthomasy@ucdavis.edu
Mechanisms of Allergic Disease (Atopic Dermatitis)	Blood samples from allergic dogs and non-allergic dogs	Elia Tait Wojno, PhD Cornell University of Veterinary Medicine 607-256-5635 Edt42@cornell.edu

For more information about any of the above projects visit www.westiefoundation.org

On The Health Front

By Kay McGuire, DVM, MS

As this newsletter reaches you in December or January, much of the country is experiencing extreme weather issues. We automatically consider the extreme cold as the most threatening problem to our pet's health. The cold weather threatens human and animal physical safety due to hypothermia or frostbite, but it also drives our pets into shelter where they can be exposed to another host of potential health issues.

Tis The Season

I think most of us are aware that holiday plants and sweets can cause gastrointestinal issues and sometimes even death for dogs. Dark chocolate, xylitol found in chewing gum, raisins, grapes, onions, and turkey skin can all lead to problems. For those owners which wish to imbibe during the holidays, please be sure that your glasses are out of reach of your pets. Alcohol toxicity is a real thing in pets too!

While Christmas trees shed needles, packages most often have ribbon, and ornaments break and are hung with nice little wires which may be appealing. Personally, I have removed objects you would not imagine from dog and cat bellies. Electrical cords may also be tempting, especially to young animals.

If the weather includes ice and snow, be sure to cover the dog's feet to prevent slashed paw pads and the exposure to the rock salt on the ice. Cats like to sleep under the hoods of

warm car engines so announce your approach by knocking on the fender.

While each of these things seems logical, it never hurts to reacquaint yourself with these dangers.

Grants 2018

Changing the topic to how the WFA granted funds in 2018, \$20,000 was pledged to a grant through Cornell University. Dr. Elia Wojno is leading the study trying to discover the genetic link to atopic dogs. If study is successful, we should be able to predict a puppy's future allergic response. This would allow breeders to make more informed decisions with their dogs at an early age. The New Zealand West Highland Terrier Club's donation to the WFA accounted for 50% of the grant. **We are in need of blood samples from both allergic and normal dogs.** Please contact me at health@westiefoundation.org for information on how to help. This grant is currently covering the cost of blood shipping.

Other grant support went through the Canine Health Foundation for studies in Lymphoma and Inflammatory Bowel Disease. Please see the article in this issue on Inflammatory Bowel Disease and how it might affect your Westie.

Lastly, for the owners that have dogs with Pulmonary Fibrosis (*Westie Lung Disease*) or have lost dogs affected with this terminal disease; there is a promising study involving a possible treatment protocol that may not only support affected dogs but also improve their condition. There is a grassroots fundraising effort to support this work through a T-shirt sale and a "Go Fund Me" drive. Please see the article in this newsletter. The WFA commends this dedication and is excited to see this study come to fruition. The link to that fund drive is:

https://www.gofundme.com/wfa-pulmonary-fibrosis-drug-study?fbclid=IwAR2MWKOwyfCh3ShyFEy1l7ptTes8F6jMXya_ccakY4CcoHirQr8bbAynKUK

As always, we welcome questions and want to hear of topics which are important to you. Please contact us through health@westiefoundation.org. I hope everyone has a safe and healthy holiday season.



Digestive System

Inflammatory Bowel Disease (IBD)

By John Robertson, VMD, PhD

Westie Health E-Book

Inflammatory bowel disease is an immune related disorder in which the intestines are chronically or intermittently inflamed. A synonym for inflammatory bowel disease that is abbreviated the same way is ‘irritable bowel disease’. Affected dogs may be presented with a history of vomiting, diarrhea, weight loss or a combination of these signs. There is a great deal of variation in the severity, duration, response to therapy, and long-term effects of IBD among dogs.

While IBD exists in different forms, the most common is lymphocytic-plasmacytic enteritis (*Figure 1*), which means that the inflammation of the small intestine (*enteritis*) is associated with increased numbers of two white blood types that are linked to the immune system (*i.e.*, *lymphocytes and plasma cells*). These are the primary immune cell types that are identified in biopsies of the affected sections of the small intestine. Lymphocytes are the cells that detect and kill viruses, fungi, and even tumor cells. When they are exposed to infectious agents, including bacteria and some complex molecules like foreign proteins and complex carbohydrates, they can transform into cells that produce antibodies. These cells are called plasma cells. Lymphocytes also interact with other immune and inflammatory cells to create the body’s active defense system that helps protect people, dogs, and other animals against disease.

IBD also can affect other parts of the dog’s gastrointestinal tract. For example, the condition known as lymphocytic-plasmacytic colitis (*Figure 2*) primarily affects the colon (*a portion of the dog’s large intestine*). There also is a rare condition characterized by inflammation caused by a different type of white blood cell. This condition, called granulomatous enteritis/gastritis, affects the small intestines and/or stomach (*Figure 3*).

Canine IBD, especially granulomatous enteritis/gastritis, is similar in some respects to the human disorder, known as Crohn’s disease. Humans with Crohn’s disease experience many

of the same symptoms as dogs with IBD and are often treated in the same manner. In fact, much of our veterinary knowledge of IBD comes from research on Crohn’s disease using dogs and other animals with spontaneous and experimental disease as translational animal models. Because Crohn’s disease is thought to have a genetic component, veterinary researchers are examining the same possibility in dogs.

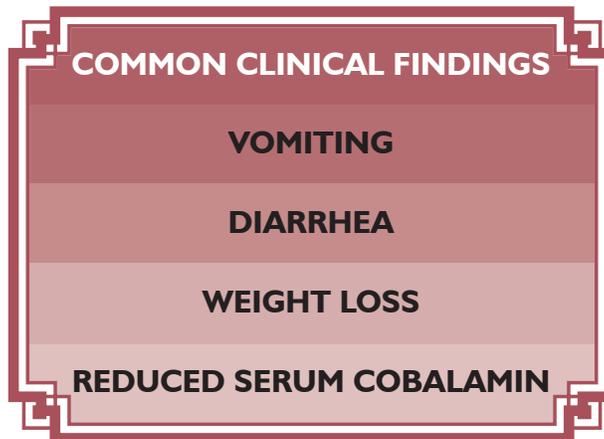
How Does A Dog Develop IBD?

Over the past few decades, several theories have been proposed regarding the cause of IBD. These include vascular

abnormalities that disrupt the function of the intestines, overproduction of mucus, an overactive gut, an infectious agent, or a dog with the equivalent of ‘hyperactivity disorder’. Currently, it is understood that IBD is an immune-related disorder, with strong evidence for a genetic predisposition in some breeds and alterations in the bacterial flora in the intestines, otherwise known as the microbiome. For example, single nucleotide polymorphisms have been identified in genes that encode for specific innate immune factors in German Shepherds

(*Allenspach et al, 2010*). There also is evidence for a shift in the bacterial populations in dogs with intestinal inflammation from gram-positive to gram-negative organisms, although at this point it is unknown if these changes are the cause or the result of the inflammation.

In a healthy dog, the small and large intestines, which includes the colon, have their own local part of the immune system. This purpose of the immune system in the gastrointestinal tract is to protect the body against viruses, bacteria or other antigens (*unwelcome outsider proteins and complex molecules*) that may be consumed in the dog’s food and water. The healthy intestinal tract is inhabited by a wide range of bacteria, many of which are important for the health of the dog. These ‘resident’ bacteria, otherwise known as normal flora, help restrict the other microbes and antigens to the lumen of the intestine; in essence,



(Continued on page 5)

the resident bacteria serve as a barrier against the unwanted microbes and antigens from gaining access to the circulation. Under normal circumstances, the intestinal immune system ignores the resident bacteria, allowing them to do their job.

However, in animals with IBD, a problem has developed in one of three areas: the local intestinal immune system or its regulation (*the body may be attacking itself or the resident bacteria*), the integrity of the intestines themselves (*through some type of injury*), or the balance of normal flora in the intestines has been disrupted. Any of these problems can trigger an unwanted immune response that becomes excessive and self-perpetuating.

What Are The Clinical Signs Associated With IBD?

The most prominent clinical signs in IBD are vomiting, diarrhea and weight loss. In general, dogs in which the small intestine is affected have large volume diarrhea, vomiting and weight loss, whereas those with involvement of the large intestine are constipated, strain or frequently defecate small amounts of feces containing blood and mucus. Often the clinical signs seem to come and go randomly, particularly in the early stages of the disease. During that time, affected dogs may appear perfectly healthy except for a change in stool consistency and frequency. A common effect of gastrointestinal inflammation is failure to absorb cobalamin (*vitamin B12*), a vitamin that has an important role in many biochemical reactions. Consequently, serum concentrations of cobalamin often are used to characterize the severity of the disease process. As cobalamin is absorbed in a specific segment of the small intestine, abnormal serum concentrations of cobalamin also help to localize the disease.

If the disease is undiagnosed or left untreated, some dogs may lose weight, and develop vitamin and mineral deficiencies that manifest as malnutrition. Another long-term problem that can occur is lymphangiectasia (*dilation of lymphatic vessels*), which can eventually result in significant protein loss and the development of tissue masses in the affected area.

How Is IBD Diagnosed?

The diagnosis of IBD is made by eliminating other possible causes for the dog's clinical problems. Because similar clinical signs (*vomiting and diarrhea*) occur with intestinal parasites, food allergies, dietary changes, stresses associated with moving/traveling/boarding, and even changes in household occupants (*like the arrival of new babies*), these must be ruled out first using a battery of diagnostic tests. For example, a fecal test will be performed to help rule out the potential role of parasites, such as *Giardia*. Blood work will be performed, and may reveal an increased population of immune related cells, indicating inflammation. Abdominal ultrasound and xrays, taken either with or without a concurrent barium enema, may provide information about the status of the intestine. While both approaches may reveal other abnormalities, neither is very helpful in making a diagnosis of IBD, but may reveal other problems.

An important diagnostic test used to diagnose IBD is a thorough examination of the intestines with a flexible videoendoscope. A videoendoscope is a long cable with a camera on one end and a viewing port on the other. The camera-end of the videoendoscope is passed into the dog's gastrointestinal tract to allow the veterinarian to view the tissue lining the inside of the intestine and to take

(Continued on page 6)

Lymphocytic-plasmacytic enteritis



Figure 1 - The most common form of inflammatory bowel disease affects the small intestine (enteritis).

Lymphocytic-plasmacytic colitis



Figure 2 - This form of inflammatory bowel disease primarily affects the colon (colitis).

Granulomatous enteritis and gastritis



Figure 3 - This rare form of inflammatory bowel disease affects the small intestine and or stomach (enteritis and gastritis).



a biopsy, if necessary. In a 2015 study, Slovak and colleagues developed and prospectively validated an endoscopic scoring system for veterinarians to use to assess the severity of disease in dogs with IBD.

Having identified inflamed areas such as this, the veterinarian can obtain small samples of the tissue using a special biopsy instrument that is passed through the length of the videoendoscope and controlled from the outside. This procedure requires sedation, anesthesia, and is invasive, time-consuming and can be expensive. The biopsy samples are placed in a tissue fixative and prepared for microscopic examination by a veterinary pathologist, who will determine if they contain an excessive number of immune cells. It is important for the pathologist to have access to several biopsy specimens, as the inflammatory response either may be localized or diffuse. If the microscopic findings do not correlate with the dog's clinical signs and other findings, a full-thickness intestinal biopsy may be obtained during more invasive exploratory abdominal surgery. This approach allows the pathologist to more fully evaluate the intestine for changes in the small intestinal villi or mucus and goblet cells in the large intestine. For some affected dogs, this is the only way a definitive diagnosis of IBD can be made.

A major differential diagnosis in dogs with some of these signs is a specific cancer affecting the intestine called malignant lymphoma. Making this diagnosis requires collaboration

between the clinical veterinarian and a skilled pathologist, as the most common features of this neoplastic disease is the presence of an increased number of abnormal lymphocytes in the biopsy tissue. A major differentiating feature of IBD is the presence of mixed populations of normal lymphocytes, plasma cells, and sometimes cells like neutrophils and eosinophils (Craven, et al, 2004). If there is any doubt about the diagnosis, it is an excellent idea to obtain a second opinion from another veterinary pathologist.

A veterinarian may also use the canine IBD activity index to "score" a patient's clinical signs and determine the severity of the disease (Jergens 2004; Jergens et al, 2003, 2010). Using this approach, the veterinarian assigns a number from 1 to 3 for each of six clinical signs: attitude/activity, appetite, vomiting, stool consistency, stool frequency and weight loss. The total score is used to determine if the disease is considered clinically insignificant, mild, moderate or severe. This index is based on similar approaches designed to quantify Crohn's disease in humans and can be used to assess a patient's progress with treatment.

Although routine blood tests typically are not very helpful in making a definitive diagnosis of IBD, the low serum protein and cholesterol concentrations that typically are measured in dogs with IBD provide evidence of a protein-losing intestinal abnormality. While this is not a way to definitively diagnose IBD, this is certainly one of the major reasons routine bloodwork is performed in patients with chronic gastrointestinal signs. Other abnormalities that may be identified in a small number of dogs with IBD are decreased numbers of circulating platelets; this abnormality was present in 2.5% of affected dogs in one study (Ridgway, et al, 2001). Treatment of these dogs for IBD resolved the low platelet count. In another case report, two dogs were identified with anemia, presumably due to blood loss through the gastrointestinal tract (Ristic, et al, 2002).

Treatment Of IBD

Unfortunately, relatively little is known about the effectiveness of particular treatments for IBD. As a result, treatment is based on empirical evidence and the clinical experience of the veterinarian. Treatment of IBD is usually multifaceted and will likely include a combination of diet changes, antibiotics and immunosuppressive drugs, including the use of corticosteroids such as prednisone. Management of dogs with IBD using medications alone is not recommended and usually is of limited value.

DIETARY CHANGES: One of the most important components of treating a dog with IBD is to change the dog's diet. This can be done by switching to a completely different diet, to reduce exposure to certain antigens that might be present in the current

(Continued on page 7)

feed. Similarly, commercial diets may be fed that contain hydrolyzed proteins that are smaller than typical proteins so as not to be recognized as antigens. Many veterinarians recommend feeding a highly digestible, rice-based diet that contains readily digestible fats and restricted amounts of fiber. Other dietary changes that can be made include altering the relative levels of omega3 and omega6 fatty acids (*to reduce inflammation*), and feeding prebiotics, such as inulin, or probiotics, such as Lactobacillus. The positive results obtained in recent studies in which dietary modifications were made in dogs with lymphocytic-plasmacytic enteritis underscores the importance of restricting exposure to antigens; in those studies, more than 60% of dogs responded positively and many did not require prolonged treatment with immunosuppressive drugs (Mandigers et al, 2010; Luckschander, et al, 2006).

ANTIBIOTICS: Antibiotics are administered to dogs with IBD in the hopes of reducing the amount of bacterial antigens present in the intestinal lumen and to control any bacterial overgrowth that might exist. Regardless, the aim is to reduce the intestinal immune response and local inflammation that are associated with IBD. The most commonly used antibiotics are tylosin or metronidazole, which in addition to its antibacterial effects also may help modulate the immune response. The beneficial responses that occur in some dogs with antibiotic therapy strongly suggest that these animals have what is called antibiotic-responsive enteropathy.

IMMUNOSUPPRESSIVE DRUGS: Based on the apparent role played by the immune system in the development of IBD, corticosteroids are given to suppress this response. Unfortunately, administration of these drugs is associated with a variety of ill effects, including gastric ulcers, increased appetite, increased urination, obesity, muscle weakness, and development of diabetes. Consequently, veterinarians are interested in pharmacologic agents that modulate the immune system, but cause fewer side effects. Because similar problems occur in human IBD patients administered corticosteroids, a relatively new drug called budesonide has been developed which is as effective as another commonly used corticosteroid, prednisone. In a recent clinical study comparing budesonide and prednisone in 40 client-owned dogs, Dye et al (2013) reported that both drugs resulted in similar remission rates (>75%) but the frequency of adverse effects also was similar between the groups.

If the response to corticosteroid therapy is poor, many veterinarians also use

azathioprine, cyclosporine A, and/or mycophenolate mofetil, immunosuppressive drugs sometimes used to treat autoimmune diseases and cancer. The most common side effect of treatment with azathioprine is bone marrow suppression, whereas gastrointestinal side effects tend to occur with the use of cyclosporine A and mycophenolate mofetil. In one study, Allenspach and coworkers (2006) administered cyclosporine A to 14 dogs that had not responded well to corticosteroid therapy, and reported concurrent improvements in clinical signs in 12 dogs and a decrease in the number of lymphocytes in intestinal biopsies obtained from these animals.

COBALAMIN SUPPLEMENTATION: Human patients with chronic gastrointestinal diseases often require monthly injections of vitamin B12 to address the low circulating concentrations of this vitamin, and a similar situation exists in dogs with chronic enteritis, such as IBD. In a 2016 study, Toresson and colleagues studied 51 dogs with chronic enteritis and low serum cobalamin concentrations, and reported that oral administration of cobalamin effectively normalized the concentrations. While these results are promising, the authors suggested that more in-depth studies need to be performed before oral supplementation can be recommended as part of the routine treatment for affected dogs.

It is critical for owners of dogs with IBD to realize that managing this disease requires a lifelong commitment. The prognosis for a dog with IBD depends on the severity of the disease and the progression at the time of diagnosis. While a change in diet and close monitoring of the dog may be all that's needed to manage many affected dogs, for others the situation may be quite different. Therefore, it is important for owners to be aware that this is a disease that is unable to be cured, instead it can be managed long-term, with the goal of achieving remission.



(Continued on page 8)

Current Research About Inflammatory Bowel Disease

Because IBD occurs in a variety of breeds, including Yorkshire and Soft Coated Wheaten Terriers, the disease may be of increased interest to Westie owners. In this section, we summarize the results of two recent studies about this important disease.

Pérez-Merino EM, Usón-Casaús, JM, Zaragoza-Bayle C, et al. *Safety and efficacy of allogeneic adipose tissue-derived mesenchymal stem cells for treatment of dogs with inflammatory bowel disease: Clinical and laboratory outcomes.* The Vet J 2015. 206:385-390.

There is a lot of interest in using stem cells in the treatment of different diseases. One of the reasons for considering them as a possible treatment for IBD is that stem cells have been shown to exert anti-inflammatory and immune system modulatory effects in different studies. In this study, adult stem cells called derived from adipose tissue were tested for their safety and feasibility of use in 11 dogs with IBD. The dogs were administered the stem cells IV and their responses were summarized 6 weeks later. None of the dogs reacted adversely to the stem cells, and there was evidence of clinical improvement in 9 of the 11 dogs, including an increase in serum cobalamin. The investigators concluded that the stem cells were well tolerated and appeared to produce clinical benefits with severe IBD.

Rossi G, Pengo G, Caldin M, et al. *Comparison of microbiological, histological, and immunomodulatory parameters in response to treatment with either combination therapy with prednisone and metronidazole or probiotic VSL#3 strains in dogs with idiopathic inflammatory bowel disease.* PLoS One 9(4): 1-13, 2014.

Based on the alterations in the bacterial populations that exist in the gastrointestinal tracts of dogs with IBD, there is a lot of interest in the potential use of probiotics in the treatment of dogs affected with this disease. This study was performed to compare the responses of dogs with IBD to treatment with either a commonly used combination therapy (*prednisone and metronidazole*) or probiotic strains (*VSL#3*). In this study, 20 dogs with IBD were randomly assigned to each treatment group and then monitored for 2 months during treatment and 1 month later. The dogs receiving the probiotic had improved clinical scores and reduced evidence of lymphocyte infiltration into the intestine when compared to the dogs receiving the combination therapy. This initial study provides the bases for larger clinical trials to evaluate the effectiveness of VSL#3 in dogs with IBD.



Acknowledgements

Mr. Matthew Crotts, a medical illustrator in Educational Resources in the College of Veterinary Medicine at the University of Georgia, created the illustrations used in this chapter.

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Westie Owners Launch GoFundMe Page, Raise Funds For Innovative IPF Study

By Teresa Barnes

PJ Kessler is a dog owner on a mission to solve a deadly lung problem in West Highland White Terriers. Not only did she create a Facebook page for owners whose dogs suffer from pulmonary fibrosis (PF) also called Westie Lung Disease (WLD), she created a GoFundMe page [<https://www.gofundme.com/wfa-pulmonary-fibrosis-drug-study>] to help researchers study a promising therapy to treat it.



“Tyler”

Kessler understands IPF far too well. She lost a Westie 10 years ago from the deadly lung disease characterized by progressive and irreversible scarring. Dogs develop an uncontrolled cough and shortness of breath that makes walking and even eating difficult and over time robs them of their quality of life.

When her Westie, Tyler, was diagnosed in 2014, Kessler decided to take action against the devastating illness. Tyler was treated at the University of Minnesota by Lindsay Merkel, DVM and was responding well to a class IV laser therapy that was being used by Merkel to help improve Tyler’s quality of life. She knew, however, the laser wasn’t going to save him.

Kessler heard about a project being proposed to study pulmonary fibrosis and reached out to Westie Foundation of America (WFA) to confirm it. She learned the study was being coordinated by the WFA and WFA was matching a top human pulmonary fibrosis research center and a top canine research center – Yale University in humans and Tufts University in canines. The study was looking at a thyroid hormone mimetic as a potential therapy. The drug they were considering was successful in phase I clinical studies in humans and preliminary research done at Yale University pointed to the possibility that the drug could be repurposed for Pulmonary Fibrosis.

Wasting no time, Kessler shared with the WFA her wish to create a GoFundMe account to help raise the \$30,000 needed to do the study. The WFA provided details about the study and Kessler launched the page and began sharing it with her Facebook page followers.

The fund raised \$500 within the first few hours and to date, has raised close to \$11,000.

Colleen Turgeon was one of the fund’s first donors. Turgeon lost her Westie, Daisy, in 2016 to WLD and her heart still ached. “Because I watched my sweet Daisy suffer with this disease, I really want there to be a cure or at least a treatment that makes

a difference. She went undiagnosed for so long – nobody knew what she had until it was too late,” said Turgeon. “My hope for this study is that we get closer to a cure – and at least a viable option for treatment.”

Claudia Gurlock, who has a background in medical research and drug and device development, also supported the GoFundMe effort after experiencing the loss of her Westie in 2017. She joined Kessler’s Facebook group soon after the diagnosis and that is where she learned about the GoFundMe effort.

“It was quite easy to donate to the GoFundMe page. I wanted to participate and raise awareness for this horrible disease that affects our Westies,” Gurlock said. “I hope that the study will be able to provide data showing that the use of this thyroid medication on dogs diagnosed with WLD is successful and may stop the progression of the disease, slow the progression, or cure it. Ultimately, it would be wonderful if it could be a precursor to human drug studies for IPF.”

Some Westie owners are reaching out to friends and family to help raise the funds needed for the study and others are asking their co-workers. Jesse Torres felt so strongly about the funding campaign, he placed a cup decorated with a photo and story of his dog, Cody, who suffers from WLD in his workplace. Torres office staff have donated \$100 and counting.

Kessler has re-launched a tee-shirt sale to add to her GoFundMe efforts to fund the study. The Bonfire WLD Warrior Club shirt drive offers Westie adorned tee-shirts for sale.

With any luck, Kessler plans to complete the funding needs for the study by raising the additional \$19,000. “We need a cure for this disease that takes so many Westies lives every year. I am committed to helping find a cure,” Kessler said. “It absolutely breaks my heart that so many Westies are dying daily from this horrible disease.”

WFA’s President, Bebe Pinter says Kessler’s effort has been hugely successful regardless of the amount of money it raises. “We are happy to see this effort, led by PJ and funded by Westie owners. It demonstrates what we always knew was true: There is no better breed than the West Highland White Terrier and the people who own and love them are exceptional in their commitment to the health of their dogs. They passionately go after opportunities to help their dogs and our Westie breed.”

(Continued on page 10)

(GoFundMe Page continued from page 10)

To join the closed Facebook Westie IPF/Westie Lung Disease group, visit www.westielungdisease.net and ask to join the group.



“Dr. Merkel and Tyler”



“Tyler”

(Continued on page 12)

A year ago, a study was published on a promising new drug. The headline read: “Thyroid hormone therapy heals lung fibrosis in animal study.” It was published by a renowned scientist at Yale, Naftali Kaminski, MD, in *Nature Medicine* and entitled: **Thyroid hormone inhibits lung fibrosis in mice by improving epithelial mitochondrial function.** To read the study, visit: <https://www.nature.com/articles/nm.4447>

The Yale team led by Kaminski took a look at all of the genes expressed in the lungs to see which genes were increased in them. They found that one gene that was increased also has a role in activating the thyroid hormone.

The curious researchers decided to examine the link between the hormone and IPF. When the team used an aerosol version of the hormone, it enhanced the resolution of fibrosis and reduced their fibrosis compared to healthy controls. The researchers also happened upon something unexpected: It has recently been suggested that in fibrosis, mitochondria, or small organelles that regulate cell metabolism – don’t function properly.

The team found the use of the thyroid hormone returned mitochondrial function to normal in the cells that line the air sacs in the lung. The team believes that this process of normalizing metabolism protects the cells from damage and allows fibrosis to resolve.

Kaminski said they needed to do further study to see if there was a role for this thyroid hormone in the treatment of Pulmonary Fibrosis (PF). The drug wasn’t new, but it was a new concept in the treatment of fibrosis. The drug, thyroid hormone mimetic, Sobetirome, is considered to be safe in humans and may represent a promising and innovative idea for a study of a deadly lung disease that claims the lives of many West Highland White Terriers around the world.

Enter the WFA.

The WFA’s Communications Vice President and Board of Directors member, Teresa Barnes, knew Kaminski and reached out to him after reading about the research. She offered for the WFA to connect Yale with canine research experts at Tufts University to look at the thyroid hormone in naturally occurring IPF in Westie dogs. Kaminski accepted and within weeks, the collaboration was underway with the canine study being led by Elizabeth Rozanski, DVM, and the protocol was designed. All it needed to begin recruitment of dog patients was funding.

It didn’t take long for Westie advocate, PJ Kessler, to mobilize a group of dog owners to come to the aid of researchers by launching a GoFundMe page after she heard about the study. To date, the fund has raised a third of the money that will be required to launch the study. To donate to the fund, go to [<https://www.gofundme.com/wfa-pulmonary-fibrosis-drug-study>]. *Funds raised will benefit the WFA and go towards a pulmonary fibrosis canine study.*

(GoFundMe Page continued from page 11)

The Westie Foundation of America (WFA) serves as a catalyst for life improvement and progress in Westie health and veterinary care. We need your help to support a new study that has the ability to change the way Westies suffering from Pulmonary Fibrosis (PF)/Westie Lung Disease are treated and has the potential to greatly improve our dogs' lives. And It might even help people or cats with this condition!

We would like to get this study underway soon and need to raise \$30,000 to make it happen.

What? Pulmonary Fibrosis Study looking at new discovery of importance of thyroid hormone in treatment (link to study in Nature on the discovery: <https://www.nature.com/articles/nm.4447>)

Who? The WFA introduced two renowned research centers to look at this discovery and its potential efficacy in Westies with PF. Yale made the original discovery and Tufts has significant interest in Westies and PF. It is a match made in Westie Heaven.

Why? Pulmonary Fibrosis poses a significant burden on the quality of life of Westies that are affected and is a major cause of death in the breed. There are no therapies approved for treatment of PF in canines.

When? As soon as possible, the WFA would like to get financial support for this study to get it underway.

Where? The study will be housed at Tufts University and the University of Minnesota and dogs will be recruited for the study in the local area (unless owners from outside areas meet the logistical requirements of the study). Tufts researchers are already working with researchers at Yale to set up the study protocol and logistics – the only thing they need to get started is the funding to do the study.

Background on WFA's work in Pulmonary Fibrosis and with Canine/Human Researchers:

The WFA works with the best scientists in the world on Westie health. We have a track record of coordinating and convening the world's greatest minds in veterinary and human medicine to tackle the most burdensome diseases in our breed. In 2014, we convened the first-of-its-kind *Fibrosis Across Species* three-day conference bringing together renowned scientists and clinicians from human and veterinary medicine. The resulting partnerships and strategies continue to pay dividends on our and our partners' investment – and because of donations by Westie owners like you. As a result of the information exchanged and shared at the meeting, the National Institutes of Health identified "fibrosis across species" as a priority in human Idiopathic Pulmonary Fibrosis research efforts. In 2007, we convened the first meeting of human and canine researchers looking at naturally-occurring pulmonary fibrosis (PF) in the Westie and explored tandem efforts to attack the disease. The WFA will continue to cover new ground

and pioneer strategies and tactics to solve the most confounding issues that affect the West Highland White Terrier.

WFA Vision for PF Research to Improve the Lives of Westies:

Our vision is to expand our efforts to become a catalyst in Westie research efforts by proactively establishing research partnerships with universities, independent research centers and experts in industry including companies in the pharmaceutical, nutraceutical and medical device industries. We envision matching researchers with potential partners and resources to provide successful and sustainable Westie-related research programs.

A Partnership for Healthier and Happier Westie Dogs and Owners

Together, we can build an all-new program that will advance research to improve the health and lives of Westies. We can make Westie ownership even more satisfying and rewarding. We can challenge the current research paradigm in Westie health and accelerate progress into finding treatments and cures for our dogs and hopefully humans. We can ensure that our leaders move us quickly in the direction of success and we fully capitalize on our research efforts and partnerships to drive innovation.

Okay, you've made a donation – Thank you! How ELSE can you help Westies?

In addition to helping fund this study, we are also planning to have Westie families help determine the normal value for the 6-minute walk test in Westies! While we know this distance (which is a measurement that provides important information about progression of disease) in people and dogs, we don't know for sure about Westies, in particular. It is EASY and you can do it at home! We need both normal Westies, and Westies that been found to have pulmonary fibrosis.

What you need:

- 1) A Westie
- 2) An area to walk that is not filled with distractions, like a parking lot.
- 3) A smart phone that measures distance. You can also use an official 6 MWT app on your phone. 6MWDAPP.
- 4) Please participate, and then enter data here! <https://www.surveymonkey.com/r/SJSZGWK>

About The Westie Foundation of America

The mission of the Westie Foundation of America, Inc. is a 501 C (3) organization established to provide financial aid and other support for medical research in order to benefit the health and quality of life of West Highland White Terriers; and, to further develop and communicate information regarding the health, care, breeding and quality of life of Westies to Westie owners, Westie breeders and veterinarians. For more information visit www.westiefoundation.org.

Studying Cancer in Dogs as a Path Towards a World Where We No Longer Fear Cancer

A Contemporary Update on Canine Hemangiosarcoma

By Antonella Borgatti, Andrea M. Fahrenkrug, and Jaime F. Modiano
Animal Cancer Care and Research Program, University of Minnesota

This is an edited version of an article published in The Alpenhorn (The Official Publication of the Bernese Mountain Dog Club of America), Fall issue of 2017, pp. 64-68. Copyright for the article belongs to the Animal Care and Cancer Research of the University of Minnesota. It can be distributed and reproduced for individual use and for non-profit purposes.

What is Hemangiosarcoma?

Hemangiosarcoma is a type of cancer that arises from cells that form blood vessels, and it is one of the most aggressive cancers seen in dogs. It is estimated that more than 50,000 companion dogs develop this disease in the U.S. each year. Hemangiosarcoma occurs primarily in the spleen, followed by the heart, skin, and liver. It spreads from the initial site where it forms, and by the time the tumor is diagnosed cancer cells have likely localized to other parts of the body. Unfortunately, this disease is invariably fatal. More than 50% of dogs with this disease will die within four to six months, and almost 90% will die within a year. Surgery and chemotherapy can prolong life for dogs with hemangiosarcoma, but currently there is no cure. The frequent occurrence of this disease, along with its insidious nature and grim prognosis, has made it a research priority for our group at the Animal Cancer Care and Research Program of the University of Minnesota.

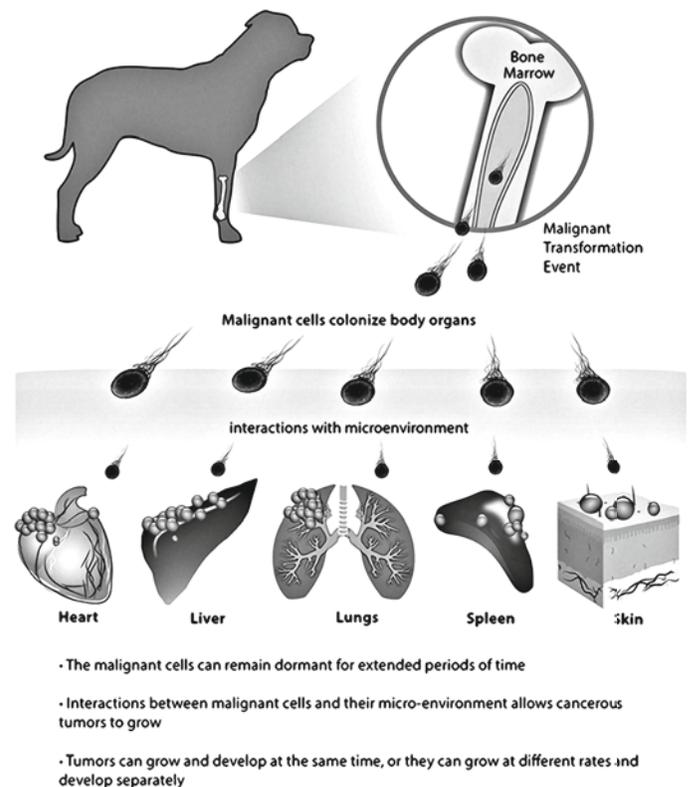
Hemangiosarcoma is more common in dogs than it is in other animals or humans. Although dogs of any age and breed are susceptible, hemangiosarcoma occurs more commonly in dogs older than 6 years and in certain breeds, such as Golden Retrievers, German Shepherds, Portuguese Water Dogs, Bernese Mountain Dogs, Flat-Coated Retrievers, Boxers and Skye Terriers, among others.

This suggests there is something peculiar about how the cells that form hemangiosarcomas behave in dogs, and that the disease could have heritable components. Yet, while certain mutations that predispose laboratory mice to hemangiosarcoma have been identified, there is no evidence to indicate mutations of the same genes contribute in a meaningful way to heritable risk of hemangiosarcoma in dogs. Nothing we know to date supports the existence of a “hemangiosarcoma gene” or genes that could be managed by selective breeding or other genetic strategies. Similarly, there is no evidence that hemangiosarcoma can be prevented by altering lifestyle behaviors, eliminating exposure to certain toys or other environmental factors, special diets, etc.

We do not completely understand why hemangiosarcoma happens. The cancer appears to start from bone marrow cells

that travel throughout the body to aid in the formation of new blood vessels. These cells can set up residence in multiple tissues, modify the local environments to sustain their survival needs, and lie dormant for long periods of time (Figure 1). Even in the absence of a spleen, the malignant cells are capable of forming tumors in other organs; therefore, removing the spleen to prevent cancer formation is not recommended.

Formation and Spread of Canine Hemangiosarcoma



Hemangiosarcoma is a cancer that does not cause pain or discomfort. It can develop slowly without interfering with normal body functions and without obvious clinical signs. Tumor cells retain the ability to reside in and possibly form blood vessels, but, unlike normal blood vessels, the tumor cells inhabit and

(Continued on page 14)

create malformed vessels where blood tends to pool and clot. Eventually, these clots obstruct the vessels, preventing fresh blood and nutrients from reaching the tumor cells and causing some of them to die. Due to this cell death, the tumor develops ruptures where blood escapes into the abdomen, heart sac, chest, or subcutaneous space, depending on the location of the tumor. While substantial blood loss can lead to signs of anemia, such as pale gums, weakness, and lethargy, the signs may be subtle and can resolve as dogs reabsorb the blood components and make new blood cells, which is one reason why hemangiosarcoma almost always goes undiagnosed until the late stages of disease. By the time the cancer is diagnosed, it is almost certainly present in other sites, even though metastases may not be visible. Nonetheless, the eventual outcome for most patients is rupture of a tumor, with acute, severe blood loss, collapse, shock, and death.

How Is Hemangiosarcoma Diagnosed In Dogs?

The first step to diagnose hemangiosarcoma in dogs showing clinical signs is a complete and thorough physical exam, which may identify a mass. If there is any reason to suspect hemangiosarcoma, the next step is to conduct imaging tests, such as ultrasound or radiographs (x-rays). If the presence of a mass is confirmed, a biopsy, where a sample of the affected tissue or the entire mass is removed and the material is examined by a pathologist, is needed to definitively diagnose hemangiosarcoma. At this time, there are no readily available, effective tests to diagnose hemangiosarcoma before clinical signs appear. It is unclear if adding imaging tests to routine well health exams is helpful to diagnose developing tumors. Careful analysis of blood samples by an experienced pathologist may hint at the presence of bleeding episodes and blood vessel abnormalities that are suggestive of hemangiosarcoma. However, this method is neither sensitive nor specific to confirm the diagnosis.

If a diagnosis of hemangiosarcoma is suspected or confirmed, the next step is to determine whether the tumor has spread to other areas (called staging). This routinely includes basic blood and urine tests, chest x-rays, and ultrasound examination of the abdomen and potentially the heart. These tests are relatively sensitive. For example, ultrasound of the heart is able to identify the presence of a tumor in the heart 65-90% of the time. However, artifacts can obscure the interpretation of any of these tests. Advanced imaging modalities such as computed tomography (CT) and positron emission tomography scans (PET-CT) are being used more commonly, and appear to be more sensitive than conventional x-rays and ultrasound.

How Is Hemangiosarcoma Treated?

As stated earlier, hemangiosarcoma in dogs is almost always fatal. Therefore, the principal goal of treatment is not necessarily

to achieve a cure, but rather to slow down or delay the spread of the disease and to prevent or delay the occurrence of life-threatening bleeding episodes. This is why surgery to remove any visible tumor mass may be recommended for hemangiosarcoma patients whose condition is otherwise stable even if there is widespread metastasis.

Without treatment, most dogs diagnosed with hemangiosarcoma will die within one to two weeks, although some can survive for several months. For dogs with hemangiosarcoma of the spleen treated with surgery, the median survival time (that is, the length of time when half of dogs receiving this treatment would remain alive) is one to three months. Adding chemotherapy to the treatment, using protocols that include the drug doxorubicin given repeatedly at two to three-week intervals, or possibly a combination of multiple drugs given daily, increases the median survival time to four to six months, making the combination of surgery and chemotherapy the preferred and most effective treatment available for this disease. Hemangiosarcoma cells in most dogs inevitably develop resistance to chemotherapy, so only 10-15% of dogs diagnosed with hemangiosarcoma of the spleen will be alive one year or longer after their diagnosis. Studies performed in the last two decades using new combinations of old drugs, immunotherapy, and new drugs, have shown no benefit to improve survival for dogs with hemangiosarcoma of the spleen as compared to conventional surgery and chemotherapy. Survival time estimates for tumors located in other organs have more uncertainty, but generally the prognosis for tumors that involve the heart, liver, and other internal organs is worse than for tumors of the spleen, and the prognosis for tumors that are localized to the skin is better than for tumors of the spleen.

Alternative and complementary approaches continue to gain popularity in the search for a cure for hemangiosarcoma, but any publicity attributing curative power to a drug after an anecdotal response should be viewed with extreme caution. As noted above, some dogs with hemangiosarcoma will live a year or longer without any evidence of disease. In rare instances dogs will live for several years without disease recurrence. This is almost certainly due to the behavior of the tumors themselves; that is, hemangiosarcomas vary greatly, and some will show extremely slow disease progression regardless of the therapy used. Therefore, we strongly recommend options and treatment based on objective data and not on anecdotal information that creates false hope and unrealistic expectations in both pet owners and their veterinarians.

Hemangiosarcoma is a devastating disease. And while there is no cure, our research is showing promising results in the areas of treatments and early detection. This promise gives us hope that we are indeed closer to creating a world where we no longer have to fear cancer.

Canine Transitional Cell Carcinoma (TCC) / Urothelial Carcinoma (UC)/Bladder Cancer in Dogs

New research provides an opportunity for early detection in the West Highland White Terrier.

Matthew Breen PhD CBiol FRSB, Oscar J. Fletcher Distinguished Professor of Comparative Oncology Genetics, Shelly Vaden, DVM, PhD, DACVIM Professor of Internal Medicine, North Carolina State University, College of Veterinary Medicine, Raleigh, NC

The opinions expressed in the article herein are those of the authors and not necessarily of the editor or the Officers or Directors of the Westie Foundation of America, Inc. (WFA). The WFA does not sell or promote products discussed in the newsletter.

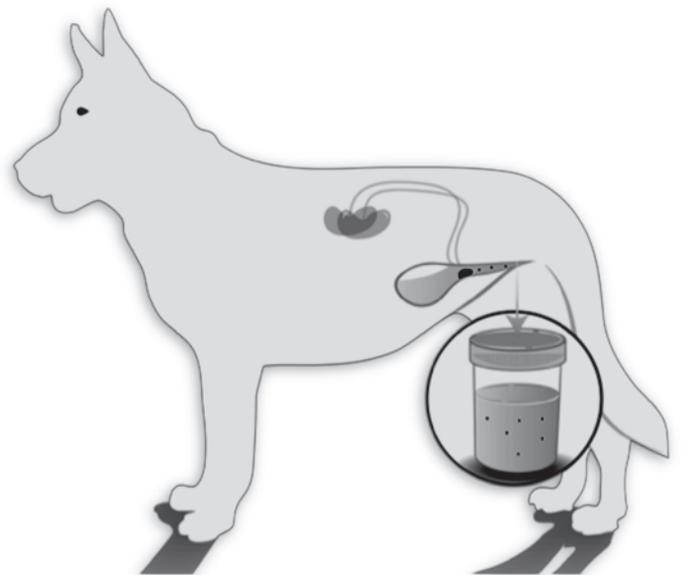
Canine TCC/UC/Bladder Cancer.

Canine transitional cell carcinoma (TCC), also known as urothelial carcinoma (UC), is the most common cancer of the canine urinary tract (1). Across all breeds the cancer represents an estimated 1-2% of all canine cancer, and with over 6 million cancers diagnosed in pet dogs each year in the US, the number of canine TCCs/UCs is therefore estimated to be 60,000-120,000. However, a group of breeds, including the West Highland White Terrier, have a much higher chance of developing the cancer. TCC/UC is generally a disease of mid to late life, with over 90% of cases occurring in dogs age 6 years and older. TCC/UC affects the bladder, urethra, and kidneys of male and female dogs, and also the prostate of males. Clinical presentation of advancing TCC/UC is shared with other much more common urinary tract disorders, including cystitis and prostatitis. These may include one or more of the following: straining to urinate; repeated frequent attempts to urinate; blood in the urine; and bacterial infection.

TCC/UC is most often detected in the trigone of the bladder, a triangular region of smooth mucosa inside the dorsal wall of the neck of the bladder. Any thickening of the bladder wall in this location can lead to partial or complete obstruction of urine entering the bladder from the ureters, which may lead to kidney failure, or exiting the bladder through the urethra (2).

How Is TCC/UC Currently Diagnosed?

A common route to diagnosis of a TCC/UC is one in which the dog is first taken to a veterinarian to assess the likely cause of the urinary tract symptoms stated above. In most cases the dog is then treated for the above symptoms, on the assumption that there is a non-malignant cause. It is common for these symptoms to initially be managed with repeated cycles of urine culture followed with antibiotic administration, and sometimes anti-inflammatory medications over several months. While this treatment approach may provide temporary relief of the symptoms, the underlying cancer causing these symptoms is still progressing. Consequently, during the time that the dog is being treated for the symptoms, the tumor can develop into a more



advanced state, becoming larger, potentially invading the muscle wall, and also having a greater chance of spreading to other parts of the dog's body (metastasis). When repeated treatments for the symptoms fail to fully resolve them, other conditions are considered and the dog is then evaluated for the presence of a TCC/UC, usually via urine cytology, abdominal ultrasound, and/or cystoscopy.

Where a mass is detected, it is recommended that a biopsy be taken and submitted for a histopathology evaluation, which serves to confirm the diagnosis of a TCC/UC and may also indicate if the mass has invaded the muscle wall. Further imaging and evaluation of local lymph nodes may be performed to assess the spread of the disease. Currently, at the time of diagnosis over 90% of cases of canine TCC/UC are of intermediate to high-grade and invasive (3). Superficial, low-grade tumors are very uncommon. In addition, at the time of diagnosis, ~20% of canine TCCs/UCs have already spread to other parts of the body (2).

(Continued on page 16)



The high predominance of advanced tumors detected by conventional means may reflect the prolonged time taken to diagnose the tumors in most cases.

How Is TCC/UC Currently Treated?

Currently, once finally diagnosed, treatment of canine TCC/UC most commonly includes the use of chemotherapy, cyclooxygenase inhibitors, and combinations of these drugs. Where single agent therapy is used, the proportion of dogs entering remission is generally low (<20%), although this is increased to 35–50% with combined chemotherapy and cyclooxygenase inhibitors. While less common than drug based intervention, surgery and radiation therapy are also used where appropriate (1). Regardless of the common drug treatment option used, median survival of treated dogs with TCC/UC is currently ~7-9 months.

What Is The Challenge?

Finding abnormal epithelial cells in urine sediment, or in samples obtained by traumatic catheterization, prostatic wash, and/or fine needle aspiration is used to support the diagnosis of canine TCC/UC (1,4,5). Cytological analysis of epithelial cells, however, may be misleading. For example, benign epithelial cells can resemble malignant cells with variation in cell size, and an increased number of basophils may be present after prolonged contact with urine or secondary to an inflammatory condition (6). Fine needle aspiration of tumor tissue carries the risk of

disseminating tumor cells along the needle tract and so should be performed with caution (7,8). Currently, clinical diagnosis of canine TCC/UC requires comprehensive diagnostic workups, including blood test, urinalysis and diagnostic imaging, in addition to cytological examinations of tumor cells by skilled clinical pathologists, and histopathology of a biopsy specimen.

Regardless of the diagnostic process used, most TCCs/UCs currently go undiagnosed until they are at an advanced clinical stage and so are associated with guarded-poor prognosis. Improved methods for earlier and less invasive detection are needed. Detection of the presence of a TCC/UC earlier in the course of disease would allow appropriate intervention sooner, which is expected to improve quality of life and extend survival. At the very least, earlier identification of the presence of a TCC/UC as the underlying cause of the common symptoms would avoid prolonged delays in detecting the cancer, expediting treating of the cancer and not just the symptoms.

The availability of a reliable, non-invasive diagnostic test for canine UC/TCC is a paramount need, as is the availability of a means to reliably detect the presence of a TCC/UC early in the course of the disease.

What Is The New Opportunity For Early Detection Of Canine TCC/UC?

In two recent independent studies, performed by research teams at North Carolina State University (NCSU) (9) and the National Institutes of Health (NIH) (10), a single mutation in the canine BRAF gene was detected in pathology verified tumor biopsy specimens of canine TCC/UC. The NCSU team identified the mutation comparing the DNA sequences of all genes of the dog DNA isolated from TCC/UC tissue samples with those from non-neoplastic tissues. The NIH team identified the mutation by looking at RNA sequences in affected tissues. The discovery of the same mutation independently by two groups using two different approaches provides cross validation of the data.

TECHNICAL DETAILS. *In the canine genome sequence at nucleotide position 8,296,284 on dog chromosome 16, the DNA nucleotide is a "T", but in the tumor cells of 85% of cases of TCC/UC, this base has mutated to an "A". The result of this single mutation is one amino change in the BRAF protein; the amino acid is supposed to be a valine, but in the tumor cells it is a glutamic acid. This mutation is located in the activation segment of the kinase domain of the BRAF gene and the change in this one amino acid produces a mutated protein with increased kinase activity. The consequence of this change is that it signals the cells to proliferate, leading to the development of a tumor.*

(Continued on page 17)

(TCC/UC/Bladder Cancer in Dogs continued from page 16)

The NCSU team showed that the BRAF mutation was not present in numerous other canine cancers and in non-neoplastic bladder tissues, including inflammatory bladder tissue and polyps. In a follow up study the team at North Carolina State University developed a rapid and highly sensitive test to detect the presence of this mutation in cells shed into the urine (11). Importantly, the new test is not affected by the presence of bacteria or blood in the urine and provides a highly effective means to detect the presence of malignant TCC/UC cells. Dr. Breen's lab at NCSU has been randomly screening urine specimens from dogs over age 6 years, from breeds considered at high risk of developing a TCC/UC, including Westies.

The research team has already identified the presence of a suspected TCC/UC before the dog had any clinical signs of the disease. Subsequent examination of these dogs by their veterinarian, followed by high-resolution ultrasound, identified a very small mass. In these cases, dogs that scored positive for the presence of a BRAF mutation in their urine subsequently progressed to develop clinical signs over the following months. This is a very exciting step forward for the earliest detection and treatment of dogs with TCC/UC.

CADETSM BRAF Mutation Detection Assay For Early, Fast, And Reliable Detection Of Canine TCC/UC In Free-Catch Urine.

Sentinel Biomedical Inc. was founded by Dr. Breen's team at NCSU to allow this test to be made widely available across the nation. The team is developing a series of rapid tests to provide dog owners and veterinarians with access to reliable early CAncer DETection in pet dogs. The CADETSM BRAF Mutation Detection Assay is the first early detection system for TCC/UC.

The CADETSM BRAF Mutation Detection Assay was designed specifically to identify tumor cells carrying the BRAF mutation, which is present in 85% of all TCC/UC cases. The test can detect as few as just 10 mutant bearing cells in a urine sample and has been detecting cases several months before any clinical signs associated with the cancer become evident. This enables owners of dogs that test positive to follow up with their veterinarian and seek the most appropriate treatment very early in the course of the disease, which is expected to improve both the quality and duration of the dogs' lives. Unlike previous and less discriminatory tests for canine TCC/UC, the CADETSM assay is unaffected by the presence of blood, protein, or bacteria in the urine.

Importantly, in all cases that have subsequently had a biopsy of a visible mass for pathology evaluation, there is 100% concordance between the presence of a BRAF mutation detected

in free-catch urine and subsequent confirmation of a TCC/UC in the biopsy of the mass. In contrast, this test does not have false positives; in studies of hundreds of controls, a BRAF mutation has NOT been detected in specimens from dogs that were shown to not have the cancer.

The goal of screening for early detection of a TCC/UC is to allow earlier confirmation of diagnosis and thus provide more time to treat the cancer and not just the symptoms.

How Will This New Early Detection Of TCC/UC Help The Westie?

The West Highland White Terrier is a breed with an elevated risk of developing a TCC/UC. Studies have suggested that the Westie is 3-6x more likely to develop this cancer than the general dog population. The mean age of diagnosis of TCC in the Westie is considered to be 11 years and 95% of all cases are diagnosed in dogs age 6 years and older. Approximately 1 in 20 Westies with TCC/UC develop the cancer when under age 5 years. As with all dogs affected by TCC/UC, the majority of tumors in the Westie are detected in the bladder. The ability to reliably detect the presence of a TCC/UC earlier in the course of disease provides more time for the dog to be treated for this cancer.

Starting at 6 years of age, we recommend that urine samples be periodically collected from Westies and submitted for BRAF mutation detection. Our initial data suggest that this should be done every four months beyond age 6 years. Sentinel Biomedical have teamed with the American Kennel Club to offer an annual subscription for the CADETSM BRAF Mutation Detection Assay. Purchase of a CADETSM BRAF Mutation Detection Assay annual subscription provides all items needed to collect and submit three urine samples from one dog to be tested over the course of a year. Owners collect urine from their dogs and ship to the Sentinel Biomedical laboratory once every four months. Results are sent back within two weeks and if the BRAF mutation is detected the owner is advised to schedule an appointment with their veterinarian as soon as possible for follow-up.

In addition to screening for pre-clinical detection, Sentinel Biomedical also offer the CADETSM BRAF Mutation Diagnosis/Monitoring Assay. This version of the assay is used by veterinarians to help identify a TCC/UC in dogs that have developed symptoms suggestive of a possible TCC/UC. Results of this test are returned to the veterinarian within 2-3 days of the sample arriving at the testing laboratory. This product is available to veterinary professionals, and to dog owners under the guidance of their veterinarian.

The CADETSM BRAF kits are very easy to use. Owners collect free catch urine from their dog(s) at home in a clean household container and pour it into one of the collection jars provided.

(Continued on page 18)

The jar is then shipped back to the lab to be tested. All packing materials and prepaid FedEx shipping labels are included with each kit.

Earlier detection will give you and your veterinarian more time to treat the cancer rather than treating the initial symptoms that emerge with the disease.

Be Part Of Nationwide Study Of Canine TCC/UC

We share the same kinds of spontaneous cancers and environmental exposures with our dogs. With highly sophisticated analytical tools now available, our dogs provide scientists with an ideal population for genetic research. Early detection tests being developed and offered by Sentinel Biomedical's CADETSM program not only provide opportunities to potentially extend lifespans of beloved pets, but also offers researchers valuable insight that can be applied to benefit human cancer patients.

Along with each submission dog owners are offered the opportunity to be part of a large nationwide research study to investigate the genetic and environmental factors associated with TCC/UC of the bladder and prostate. This study will provide valuable data to help your breed and other breeds diagnosed with these cancers, and all participants will have access to updates of the research program to learn how their dogs has contributed.

Our dogs truly are our best friends, in the home and in the fight against cancer.



For further information about the CADETSM *BRAF* Mutation Detection Assay please e-mail CADETBRAF@SentinelBiomedical.com

Further Reading – The Science Behind The Testing.

- 1) Mochizuki H, Kennedy K, Shapiro SG, Breen M. *BRAF* Mutations in Canine Cancers. *PLoS One*. 2015;10(6):e0129534. doi: 10.1371/journal.pone.0129534. PubMed PMID: 26053201; PubMed Central PMCID: PMC4460039.
Review study at: <http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0129534>
This study reports on the presence of the *BRAF* mutation across numerous canine cancers, highlighting the high frequency of the mutation in canine TCC/UC.
- 2) Mochizuki H, Shapiro SG, Breen M. Detection of *BRAF* Mutation in Urine DNA as a Molecular Diagnostic for Canine Urothelial and Prostatic Carcinoma. *PLoS One*. 2015;10(12):e0144170.
Review study at: <http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0144170>
This study reports on the development of the *BRAF* mutation assay used to detect the presence of the mutation in urine specimens.

- 3) Decker B, Parker HG, Dhawan D, Kwon EM, Karlins E, Davis BW, et al. Homologous Mutation to Human *BRAF* V600E Is Common in Naturally Occurring Canine Bladder Cancer--Evidence for a Relevant Model System and Urine-Based Diagnostic Test. *Mol Cancer Res*. 2015;13(6):993-1002. doi: 10.1158/1541-7786.MCR-14-0689. PubMed PMID: 25767210; PubMed Central PMCID: PMC4470794.
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Let the IRS Help

By Tom Barrie

Making a contribution to the Westie Foundation should be a convenient, efficient process. In addition to the satisfaction of supporting Westie health research, one of the benefits of contributing is the income tax deduction which is allowed for charitable contributions. The 2018 tax law changes may reduce the benefits to the donor by making the standard deduction large enough that charitable deductions, with other deductions, do not exceed the standard deduction allowance. For some, the new standard deduction will make itemizing deductions of no benefit to the taxpayer.

You can usually deduct the full fair market value of appreciated long-term assets you've held for more than one year, such as stocks, bonds or mutual funds. In addition, if you donate stocks or other investments, you pay no capital gains tax.

Donating investments—especially highly appreciated securities—instead of cash can be a very effective and tax-efficient way to support a charity. Generally, if your assets have appreciated in value, it's best not to sell securities to generate the cash you need for a donation. Contributing the securities directly to the charity increases the amount of your gift as well as your deduction.

This method will maximize the effect of your gift to the Foundation by donating appreciated assets, such as stocks, bonds or mutual funds. Especially after a period of escalating stock markets, the value of many stocks will include unrealized gains. By making a donation of appreciated stock, the recipient gets the current appreciated value, and the donor is allowed the deduction for that value. No tax is due to the donor on

the appreciation – the charity pays no tax: in effect, a tax-free transaction.

Many retired individuals are faced with IRA Required Minimum Distributions (RMD). Specified amounts must be withdrawn each year or the owner faces major penalties. Again, in this case, if the owner chooses to make a donation out of this withdrawal, he should make it as a direct in-kind donation to the Foundation, avoiding personal taxes on the donation, yet fulfilling the obligation for the RMD. This process is called an IRA Charitable Rollover, and allows a donor to lower their adjusted gross income and therefore the overall tax liability.

Since fewer taxpayers are itemizing their tax deductions, it may make sense to “double-up” your contributions by making double contributions in one year.

Every Broker will have the forms on their website necessary to make a direct stock transfer, or contact your customer representative to get the information you need. Also contact

[Gary Sackett, WFA Treasurer, treasurer@westiefoundation.org]

[or Jim McCain, Donor Manager, catercain@gmail.com]
choose one for necessary information on where the donation is to be sent.

Of all the itemized deductions available to you, the charitable deduction is perhaps the most flexible in that you can control both the amount and the timing of your donations. And, as with all tax decisions, it's a good idea to meet with a tax or financial advisor to determine the best charitable-giving strategy for your situation.



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Westie Cartoon Caption Contest

Create the winning caption for this Westie cartoon. Please send your caption to bjpinter@msn.com before February 15, 2019. The winner will be announced in the next newsletter with his/her caption.

Create a Caption for this Cartoon

Copy of original watercolour by Ruth Sutcliffe, England



Winning Caption of Last Cartoon! Anne Tiessset-Miller



“Bow Meooowww!”



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