Tumors, Cancer, and Your Westie

John Robertson, VMD, PhD and
Natalie Christianson

Introduction and Overview

"Your dog has cancer." This is one of the most stressful things a Westie owner can ever hear from their veterinarian. For most people, there is an immediate concern about what it is (what kind of cancer), what to do about it (if anything), and what is going to happen to their dog. This chapter discusses cancer (also called "tumors" or "neoplasms"), how they are detected and further diagnosed, types of treatment, and what to expect if your dog has cancer. The chapter is not intended to provide comprehensive information about cancer in dogs. The best source of information about cancer in dogs and specifically in your Westie is your veterinarian. Veterinarians are extensively trained to understand how cancer develops, the factors that foster growth of cancer, and, most importantly....what to do if your Westie is diagnosed with cancer. Unfortunately, the author of this chapter knows personally about tumors and cancer in dogs and cats, and the toll it takes on owners. His best friend, Fluffer I the Westie succumbed to a tumor of the testis when he was a young boy. Experience is a terrible way to learn some things.

What is cancer and what causes it? All tissues in the body (of dogs and people alike) are made of many cells. Cells in different tissues, such as muscle cells in muscle and kidney cells in kidneys, have different architectures and functions. All of these cells started from a single cell – the fertilized egg - that gave rise to an embryo and eventually to all cells and tissues. Since every cell in every tissue came from one single cell, all cells have the same DNA, organized into genes and chromosomes in the cell nucleus. As a result, all cells are genetically identical.

During the processes of cell growth, duplication, and organization into tissues, the form and function of the cells and tissues evolves into their 'final' adult form. This process of cell evolution is called differentiation. Cell growth, replication (making more cells), and differentiation let tiny puppies grow into dynamic adult dogs.

The processes of cell growth, replication, and differentiation occur every day and throughout life. These processes are absolutely critical in repairing damage and replacing worn out tissue components. It is important to realize that the processes of growth and repair are very tightly controlled by genes in the nucleus of every cell. When these processes are working perfectly, cells that can replicate make exact copies of themselves, and other cells ensure that tissues continue to function properly.

Cancer is comprised of cells that have escaped from the normal controls of cell division, replication, and differentiation. The fundamental 'thing' that starts and fuels this out-of-control process is mutation of genes that program and control cells. Mutations (changes in gene structure and function) have an important normal role in evolution, as they provide the mechanisms needed for changes in genes to be incorporated into organisms (and eventually into species). Mutations that favor new characteristics and improve survival become permanent additions to the gene blueprint of cells ("the genome"). Mutations that damage the DNA in genes in the genome and that impair cell survival usually aren't preserved, as the cells with these profound defects die off before they make more cells.

Some mutations affect critical elements in genes that control

> Tumors (neoplasms) are groups of abnormal cells that have escaped from the normal controls of cell division, replication, and differentiation.

cell growth, replication, differentiation, and survival. It is these mutations that give rise to cancer.

Mutations can be caused by many things. Surprisingly, some mutations (favoring abnormal gene control and function) can be inherited. We know that the selective breeding of dogs for the past 200+ years has facilitated the passage of mutations favoring tumor development in some breeds of dogs, including Westies. An example of an inherited 'risk' for developing tumors is bladder cancer in Scottish and West Highland White Terriers (see Bladder Cancer in Westies and Scotties). At some point in the selective breeding of these purebreds, one or more mutations were incorporated into their genome and have been inherited ever since. Another example is lymphoma in Golden Retriever dogs. Based on breed and health club statistics, about 60% of Golden Retrievers will succumb to lymphoma or tumors of the spleen (hemangiosarcoma). As dog breeders and owners, we need to be aware of the presence of breed-associated inherited mutations linked to the development of cancer.

Many mutations are caused by exposure to excessive ionizing radiation (e.g., ultraviolet light, x-rays/gamma rays), chemicals that damage DNA (called chemical mutagens), and some very specialized viruses (called oncogenic viruses). These entities (radiation, chemicals, and viruses) are collectively referred to as carcinogenic agents. They damage DNA and genes, removing critical control elements that regulate cell replication, differentiation and survival. Dogs and people get exposed to these carcinogenic agents in the air, drinking water, in food, and by direct physical contact. Exposure is unavoidable; but our bodies and those of our dogs are very resistant to the effects of the agents, and very, very few exposures ever lead to mutations and even fewer lead to the uncontrolled growth of cells (causing cancer). Our bodies simply kill off nearly all mutated cells. Unfortunately, a few survive.

We now know that the formation of cancer begins in individual cells that acquire several mutations (either through inheritance or exposure to carcinogenic agents). These mutated cells make more mutated cells...and more mutated cells, creating a tumor. This process of evolving from one uncontrolled cell to a clinically important tumor takes months to years. So, by the time we owners see cancer in our dogs, it has been developing for a long time.

Benign tumors and malignant tumors ("cancer"): By examining small samples microscopically, tumors are classified by their growth patterns and cell architecture (see **Bladder Cancer in Westies and Scotties**) as being either benign or malignant. Benign tumors, such as warts (officially known as "cutaneous papillomas"), are characterized by excessive cell growth in a local area. Many benign tumors form discrete lumps and bumps. These are frequently treated by surgical removal, local chemotherapy, radiation, cryosurgery (freezing), or a combination of these treatments. Benign tumors usually respond very well to treatment, being well controlled for long periods of time or cured completely.

Malignant tumors are a different story. Malignant tumors are those types of neoplasms that are officially "cancer". Malignant tumors start as local uncontrolled cell clusters, but may spread (infiltrate) into the tissue around them. Malignant neoplasms may also spread to distant sites, a process called "metastasis", by way of the blood stream and lymphatic channels. Sometimes, veterinarians will use the terms "carcinoma", "sarcoma", or "round cell cancer" when discussing malignant neoplasms. These terms help define the type of tissue that the cancer originates from and relates to terminology that pathologists use when describing what they see in the tissue samples (see **Detecting and Diagnosing Tumors**).

Malignant tumors can be difficult to control or eliminate in dogs and people. One reason for this is that malignant cells tend to infiltrate normal tissues around the site of tumor growth early in the life span of the tumor. Because malignant neoplasms infiltrate tissue, they can be more difficult to remove with surgery or radiation therapy. As a result, malignant tumors frequently require extensive surgical resection, followed by additional radiation and chemotherapy to control tumor growth. Unfortunately, many malignant tumors are identified after they have grown for a while, and they may be large, highly infiltrative, or have already sent clusters of tumors cells to distant sites, like the lung, liver, brain, or bones (tumor metastases). When these malignant tumors are spread, they are more difficult, if not impossible, to get under control and to cure.

Figure 9.2 - A great time to start examining your dog is when it is three-weeks old. (Photo courtesy of Bebe Pinter and Kay McGuire, DVM, MS).

Detecting and Diagnosing Tumors

Most tumors are detected by dog owners, not veterinarians! You are your Westie's best friend and spend the most time with your dog. It is very common for owners to be the first to detect "lumps and bumps" that appear on the skin, simply by seeing them, or feeling them as they pet or groom their dog. So, Strategy #1 in fighting tumors – regularly (every day) examine all the parts of your dog you can see and feel. Early detection of tumors is always ideal, because tumors that are identified when they are small are usually easier to treat and there's a lower chance they will spread into the surrounding tissue or to distant sites.

Regular examination should start when dogs are very young and continue throughout their life (**Figure 9.1**). A great time to start examining your dog is when it is three-weeks old. This activity helps you bond with your dog and helps the dog get used to being examined; your veterinarian will thank you for doing this. Most importantly, this will help you identify abnormalities like swellings/lumps and potentially painful spots that are often hard to see because they are covered by hair or they are on parts of the dog (the belly, for example) that may not be easy to see. A good routine is to start by patting and stroking the head and face and then moving your hands down the entire body. Palpation (i.e., careful, systematic touching) should extend to the neck, under the legs, the belly and the groin. Your examination should include looking at the eyes, eyelids, ears and into the mouth. Being thorough and starting early in life are keys to success, as dogs get used to the examination as part of their daily routine (**Figure 9.2**).

Male dogs need to get used to examination of their penis and testicles; testicular tumors can cause asymmetrical (uneven) swelling of the testicles, generally in older dogs. The absence of a testicle in the scrotal sac ("cryptorchidism"), after dogs have reached 6-12 weeks old, should trigger a visit to the veterinarian. Testicles that are retained in the inguinal canal or abdomen may develop tumors later in the dog's life. Breeders

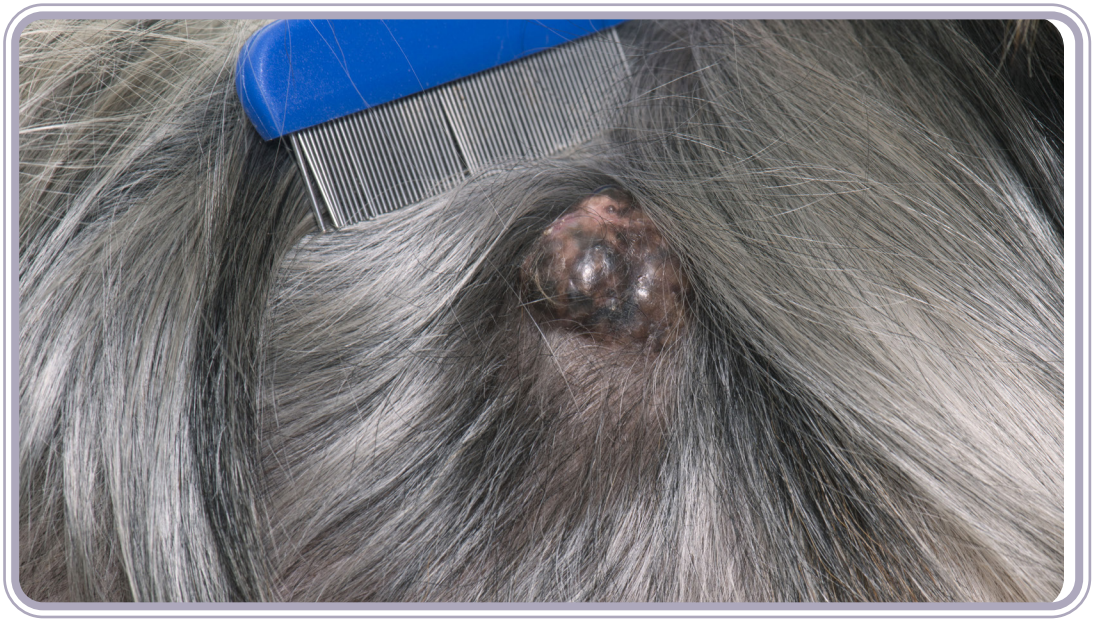

Figure 9.2 - Some skin tumors may be hidden beneath the dog's hair.

need to be especially diligent about regular evaluation of the testes of their male breeding dogs, since testicular tumors are most common in older male dogs. Neutering at a young age effectively eliminates the chance that a male dog will develop testicular tumors.

The careful examination and palpation of the mammary glands is very important, as tumors of the mammary glands are common in all breeds of dogs. Most of these tumors start as small lumps, perhaps the size of a pea, but can grow steadily larger. It is not uncommon for some dogs to have small lumps develop in multiple mammary glands over time. Approximately half of mammary gland tumors in dogs are benign and can be readily treated with surgery. However, the other half can be malignant with a potential for metastasis (spread) to other parts of the body. For these malignant mammary tumors, dogs may need additional treatment, such as chemotherapy, after surgery.

If you find a lump....see your veterinarian! There are many things, both cancerous and non-cancerous, that can cause lumps, bumps, and other abnormalities on the skin, eyes, ears, and "outside parts". Lumps that are scabbed over or which bleed easily, as an example, could be anything ranging from a localized skin infection to a tumor. You and your veterinarian then will determine the next steps to take. If your veterinarian is concerned that your Westie could have a tumor, they may recommend obtaining a diagnostic sample of the lump. This diagnostic sample could be a small needle sample ("fine needle aspirate") or a tissue biopsy. With a fine needle aspirate, your veterinarian uses a syringe to insert a needle in the abnormal lump, pulls back on the plunger to aspirate material into the needles, and then deposits that material onto a microscope slide. Your veterinarian (or a pathologist) can then examine the material with a microscope to determine whether the lump appears to be something cancerous (e.g., a mast cell tumor) or non-cancerous (e.g., an abscess).

Though fine needle aspirate sampling is relatively non-invasive, it can sometimes be tricky to obtain enough cells using this technique to definitively determine whether a lump is cancerous or non-cancerous. In this event, it may be necessary to obtain a tissue biopsy sample. Biopsies involve surgically removing a piece of tissue from the lump. This is typically done while the dog is either heavily sedated or under general anesthesia. The piece of tissue is first preserved in a solution of formaldehyde and then processed to produce a thin piece of stained tissue on a glass microscope slide. This slide is evaluated by a pathologist trained to recognize the abnormalities in cell size and architecture that differentiates normal cells from tumor cells. It is important to recognize that it generally takes 1-2 weeks to process and examine a surgical biopsy.

In most cases, a pathologist examining a biopsy sample can determine whether a lump is benign or malignant and provide a specific diagnosis (e.g., a benign cyst of the hair follicle or a malignant melanoma). If the veterinarian performed surgery in an attempt to remove the entire tumor, the pathologist will evaluate the edges of the tissue – the boundary between normal and abnormal tissue (called "the margins") – to see if the tumor has been completely removed. In most cases, surgery to treat tumors is designed to remove all tumor cells, as remaining tumor cells may regrow. In these cases, the goal is to achieve "clean" or "complete" margins, which means there are at least several millimeters of normal tissue separating the abnormal tissue from the surgical boundary.

While tumors on the outside of the body (skin, mammary glands, testes, eyes, eyelids, ears) can be easily detected by regular and repetitive examination, some tumors grow in tissues inside the body. These tumors are not easily detectable but may produce some signs that your dog needs further evaluation. Some clinical signs that may trigger further evaluation include:

- Unexplained loss of weight and changes in eating habits, including loss of appetite
- Unusual discharges from body orifices including ears, mouth, reproductive tract, or digestive tract
- Unusual behavior, including lethargy or sleepiness that is not normal for your dog
- Unusual weakness or lameness
- Pale gums or collapse
- Vomiting or diarrhea

Other changes in the normal routine of your dog that make you think "Something is not right". In fact, this is how I detected tumors in several of my dogs and cats. My dog Heidi, age 11, suddenly collapsed because a tumor in her abdomen was making hormones that interfered with blood calcium concentrations.

When you suspect that "something is not right", your veterinarian will conduct a thorough physical evaluation of your dog and possibly bloodwork to look for abnormalities that could suggest the presence of cancer. If your veterinarian is concerned that your Westie could have cancer affecting an internal organ, they may recommend additional testing like x-rays, ultrasound, or a CT scan or MRI performed by a specialist.

In many cases, this more thorough evaluation will help determine if a tumor is present, where it is located, and whether the cancer has metastasized (i.e., spread) to other

Most Common Types of Tumors
Blood/Lymph Tissue 22.6%
Urinary 17.7%
Skin 14.5%

parts of the body. This process will help you and your veterinarian determine the best course of treatment. If an internal mass is detected, veterinarians often recommend that a fine needle aspirate or biopsy sample be collected. This will be examined to determine the type of tumor and, based on its characteristics and what is known about tumors of this type, to predict how the tumor will grow and potentially spread, and which therapies might be effective.

Common Tumor Problems in Westies

A couple of generalizations about tumors in dogs will help put things in perspective:

- Tumors are more common in middle age (over 5 years old) and older aged dogs than in young dogs.
- Most tumors develop due to spontaneous and unpreventable mutations in cells; owners need to know they very likely could not have prevented the development of a tumor, except...
- Early neutering of male dogs will eliminate development of testicular tumors and may affect development of prostate problems.
- Spaying of female dogs less than one year of age will decrease the incidence of mammary gland tumors as the dog ages. Early spaying eliminates the possibility of developing both ovarian and uterine tumors, although neither of these types of tumors are common in dogs.
- Regular examinations by owners and veterinarians help detect tumors at earlier stages, when they are more likely to be controlled with surgery, radiation, and chemotherapy – the standard types of treatment.
- • Skin tumors are common in all dogs and often can be effectively treated with surgical removal.
- Malignant tumors are more difficult to treat and control, are more likely to have poor outcomes, and can be costly to manage if chemotherapy and/or radiation therapy is used.

Tumors in 62 Westies by site of occurrence; number in parentheses is the number of neoplasms (**Figure 9.3).**

- Digestive System (7)
- Endocrine System (1)
- Epithelial and Melanocytic Tumors of the Skin (9)
- Hematopoietic/lymphoreticular System, including Malignant Lymphoma (14)
- Mesenchymal Tumors of Skin & Connective Tissue (3)
- Mammary Glands (5)
- Male Genital System (2)
- Nervous System or Eyes (4)
- Respiratory System (6)
- Urinary System (11)

The most common types of neoplasms, based on percentages were: hematopoietic/lymphoreticular system neoplasms including malignant lymphoma (14/62 = 22.6%) and urinary system neoplasms (11/62 = 17.7%).

While the information in this database search is very useful for identifying overall trends in the incidence of neoplasms in dogs, it has limitations. First, only a small number of total cases are submitted for entry, and it is likely that there are many more dogs with tumors whose records are not submitted for inclusion. Second, only cases in which there has been a biopsy confirmation of the tumor type are included. Many dogs with masses may not be biopsied and their information may not end up in the database. Third, it is hard to tell if the numbers in the Veterinary Cancer Registry database represent all of the dogs at risk. There is no way to know how many Westies (or Scotties, or Cairns, or dogs of mixed heritage) are in the United States. As a result, we can only make rough estimates of 'dogs at risk' for developing neoplasms.

Breed clubs such as the West Highland White Terrier Club of America (WHWTCA) and canine health foundations such as the Westie Foundation of America, Inc. (WFA) conduct surveys to help determine the number of dogs in their breed that reside in the United States. Data from these organizations can help provide rough estimates of 'dogs at

risk' for developing neoplasms and is a great help in making more accurate data available.

Bladder Cancer in Westies and Scotties

One type of cancer that is of very serious concern to owners of Westies and Scotties is bladder cancer. The medical designation of this type of malignant cancer is "transitional cell carcinoma", also known as "urothelial carcinoma," of the urinary bladder. Bladder cancer can occur in any dog breed, but is more common in Shetland Sheepdogs, Scottish Terriers and Westies. The median age of occurrence for dogs is around 8 years old.

There are several excellent websites which discuss bladder cancer in dogs, how this tumor is diagnosed and how it is treated. While owners may wish to "Google" this subject, a more comprehensive, scientific literature review and list of references are found at the end of this section.

A brief summary of important aspects of this disease will help to alert Westie owners that their dog may have a problem. Bladder cancer develops from cells that line the urinary bladder and the kidney. There appear to be several factors that influence whether or not this neoplasm will develop. In dogs, the genome appears to play a major role, as some breeds (the short-legged Scots breeds like Westies and Scotties) appear to have a higher incidence per capita than other breeds of dogs (see below). This increased breed incidence suggests that during the development of the breed, certain mutations in the genome were acquired and linked to desirable breed characteristics. It is very likely that several mutations may be present and research scientists are actively looking for them, in order to see what is causing cancer to develop. Remember, not every dog will inherit mutations that can lead to the development of cancer, and it may take the complex interactions of several mutations to lead to the initiation and development of neoplasms.

There is also increasing evidence to suggest that exposure

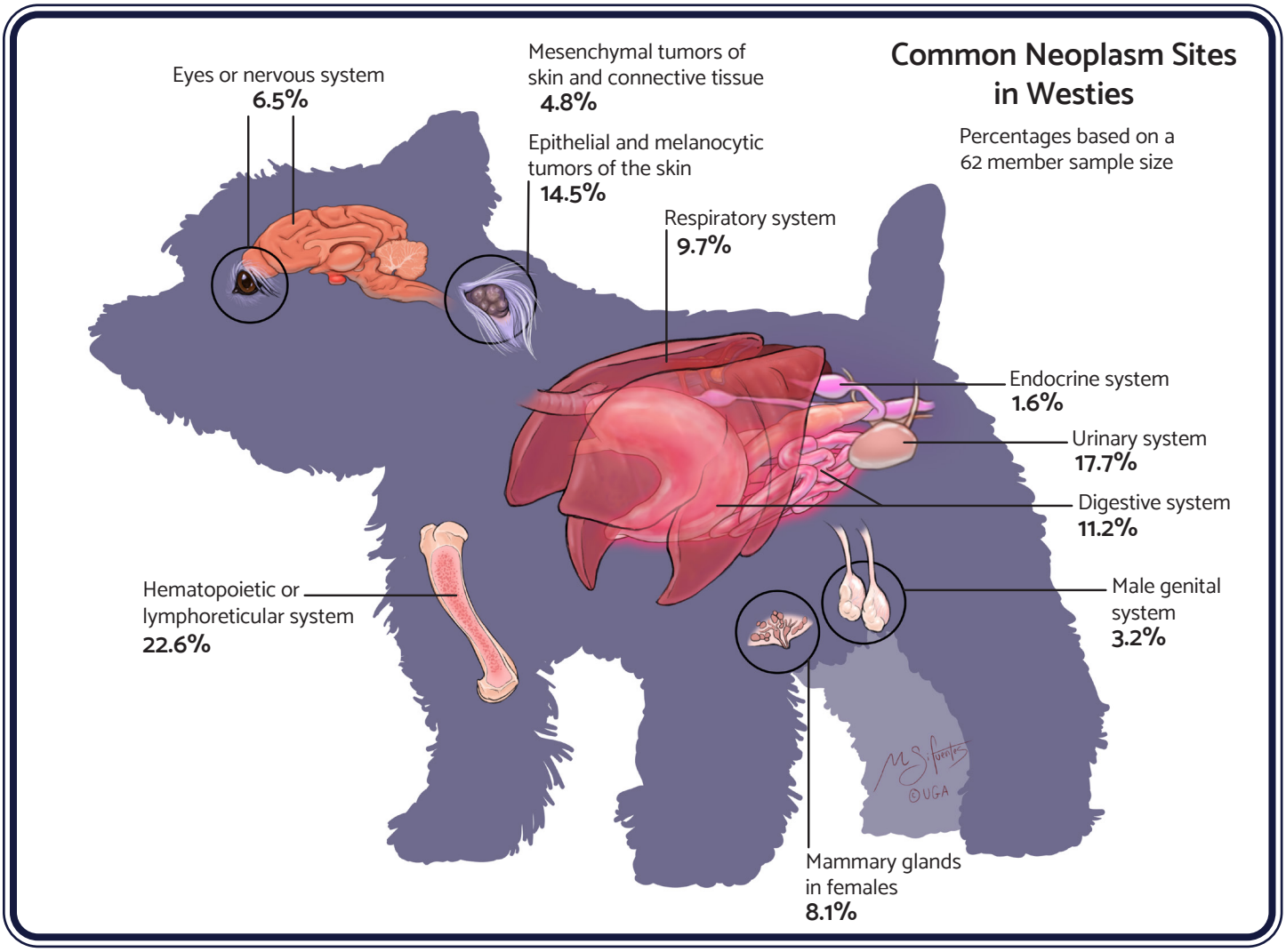

Figure 9.3 - Depiction of common places for neoplasms to arise in Westies.

to certain environmental factors may be associated with the development of bladder cancer in humans and dogs alike. Glickman and his colleagues at the Purdue University School of Veterinary Medicine have shown that repeated exposure to one type of common lawn chemical – phenoxy herbicides – may lead to an increased risk for developing bladder cancer in Scotties. Another recent study by Smith, Trepanier, and their colleagues at the University of Wisconsin School of Veterinary Medicine showed that dogs with bladder cancer were more likely to live in households with higher levels of tap water contaminants compared to their healthy counterparts.

Diagnosing Urinary Bladder Cancer in Dogs

The first clinical signs that there may a problem with the health and function of the urinary bladder may be one or more of the following:

- Difficulty urinating or straining to urinate
- Frequent attempts to urinate (a change in the pattern of urination)
- Dribbling urine
- Urinary accidents in the house in housebroken adult dogs
- Blood in the urine ("hematuria), evidenced by pink or red spots on floors and carpets

These symptoms only indicate a potential problem with the health and function of the bladder and are not specific for any one disease. For example, these symptoms might indicate bladder infection ("UTI"), the presence of bladder stones, a neurologic problem leading to altered bladder function, or the presence of a bladder tumor, among other diseases. If Westie owners detect any of these symptoms, it is important for them to take their dog to their veterinarian for further evaluation.

The veterinarian will perform a physical examination and suggest some additional tests to narrow down what is causing the dog to have symptoms of bladder disease. During the physical examination, it is very likely the veterinarian will gently palpate the dog's abdomen, paying attention for signs of tenderness, especially around the area of the urinary bladder. They will also do a rectal examination to palpate the urethra and in male dogs, the prostate. Abnormalities affecting the urethra and prostate can accompany bladder disease, or can closely mimic the symptoms of bladder disease.

The veterinarian may suggest collecting a urine sample, either by catching urine in a pan or a cup during spontaneous urination (a "free catch" specimen), by passing a catheter into the bladder, or by taking a small sample with a syringe and needle, through the abdominal wall ("cystocentesis"). Because urine samples collected with a catheter or by cystocentesis are sterile, they can be used for bacterial culture to see if there is a bladder infection present. Urine samples can also be analyzed for the presence of blood and to see what types of cells and other suspended materials are present. In some cases, veterinarians and clinical pathologists will identify clumps of abnormal cells that may indicate the presence of bladder cancer.

While taking x-rays of a Westie's abdomen can be helpful to look for bladder stones, it can be very difficult to identify masses involving the bladder itself. For this reason, if your veterinarian is worried that your Westie might have a mass in its bladder, they will likely recommend either an ultrasound or CT scan to examine the inside of the bladder. Bladder tumors can extend from the bladder itself down into the urethra, which is the tube that carries urine from the bladder to the outside world. Ultrasound and CT scans are also useful for visualizing the full extent of the tumor (**Figure 9.4**). Alternatively, your veterinarian may refer you to a specialist to have cystoscopy performed. This procedure involves passing a small camera device up your Westie's urethra into the bladder. Using this camera, the specialist can directly examine the entire urethra and bladder, looking for any tumors or other abnormalities affecting the urinary system.

Definitive Diagnosis and Options for Therapy

If these initial diagnostics confirm the presence of a mass in your Westie's bladder, the next step is to determine whether this mass is cancerous. The most definitive way to do this is to obtain a biopsy sample. Most commonly, these biopsy samples are obtained during a cystoscopy procedure, as mentioned above. This is a relatively non-invasive way to obtain samples directly from the mass without requiring your Westie to undergo a surgical procedure.

Alternatively, your veterinarian may consider doing a surgical biopsy of the bladder mass. This involves an exploratory surgical procedure of your Westie's abdomen to enter the urinary bladder, examine the mass, then remove some (or all) of the mass (depending on its location in the bladder). Whether obtained via cystoscopy or surgical biopsy, the biopsy sample is then sent to a pathologist who will examine the cells comprising the mass to determine whether they are cancerous, inflammatory, or representative of something else altogether. Both cystoscopy and surgical biopsies are performed with the animal under general anesthesia. One risk of surgical biopsies of bladder masses is that cancer cells floating in the urine can spill into the abdomen during the procedure. If this happens, those cancer cells can attach to

other abdominal organs and start growing there, leading to additional sites of cancer.

More recently, scientists have developed a non-invasive genetic test called the "BRAF" test to screen dogs for transitional cell carcinoma. Transitional cell carcinoma, also known as "urothelial carcinoma", is the most common type of cancer affecting the bladder, urethra, and prostate in dogs (**Figure 9.5**). The BRAF test looks for the presence of a mutation of the b-raf gene in the urothelial cells that line the bladder and urethra. Importantly, more than 80% of dogs with transitional cell carcinoma are affected by this genetic mutation. The BRAF test is non-invasive and is performed on a small urine sample (approximately 3 tablespoons) obtained from your dog.

A positive BRAF test, indicating the presence of a mutation in the b-raf gene, is highly suggestive that the dog has transitional cell carcinoma. However, there is a small risk of false positives, meaning that some other disease of the bladder (e.g., inflammation) can result in a positive BRAF result. On the other side of the coin, the BRAF test gives a false negative result approximately 15% of the time. In this case, the dog could have a negative BRAF test but still have transitional cell carcinoma affecting the bladder, urethra, or prostate. If your veterinarian is concerned that your Westie could have transitional cell carcinoma based on their symptoms or the presence of a mass in their urinary tract, it would be reasonable to consider submitting a urine sample for a BRAF test.

If your Westie is diagnosed with cancer of the bladder, such as transitional cell carcinoma, your veterinarian will likely discuss treatment options and referral to a veterinary oncologist for chemotherapy and/or radiation therapy. The goal of using either of these treatments is to slow further growth of your Westie's bladder tumor for a period time. Chemotherapy can also help slow down potential metastasis (spread of cancer) to other parts of your dog's body.

Many of the chemotherapy drugs used to treat bladder cancer in dogs are the same ones used to treat bladder cancer in humans. Chemotherapy works by killing cells in the body that are dividing quickly, including the cancer cells. The mechanisms by which chemotherapy drugs kill rapidly dividing cells include interrupting cancer cell division, blocking cancer cell metabolism, breaking down cancer cell DNA and genes, or poisoning other cancer cell activities.

Cancer chemotherapy drugs are usually given by intravenous (IV) injection or by mouth, or a combination of these methods. Chemotherapy may be continued for at least several months, depending on the extent of the tumor, response of the tumor to chemotherapy, and how well your Westie is tolerating his or her treatment. Most dogs tolerate chemotherapy quite well and lead normal lives during their treatment. However, because chemotherapy kills rapidly dividing cells in the body, it can also affect cells that line the stomach and intestines, as well as the cells in the bone marrow that produce white blood cells (immune system cells) and platelets.

Side effects of chemotherapy can include temporary stomach upset (i.e., loss of appetite, vomiting, diarrhea), loss of energy, and increased susceptibility to infections or bleeding if their white blood cells and platelets are affected. Typically, these

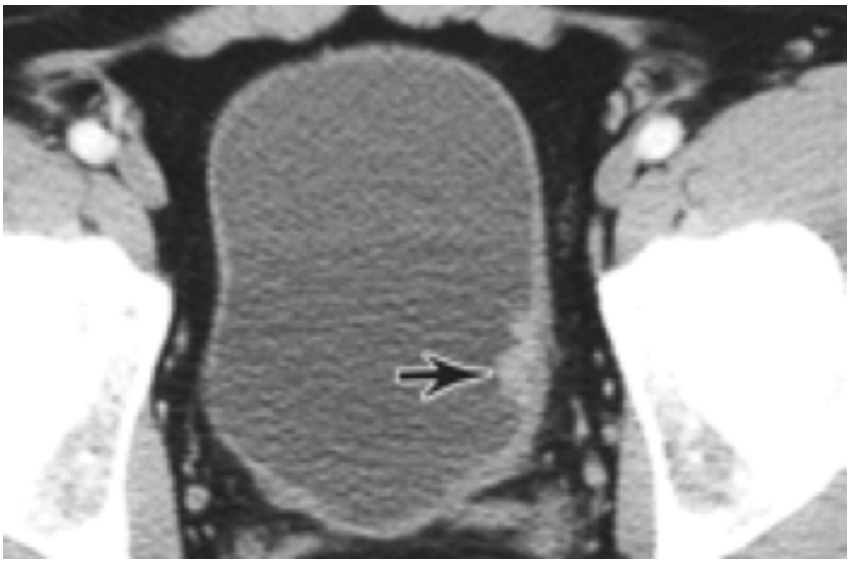

Figure 9.4 - A CT image of the urinary bladder of a Sheltie dog which was seen by a veterinarian for blood in the urine. The arrow points to a dark mass (a "filling defect") is a transitional cell carcinoma projecting into the center of the bladder.

side effects are mild and can be managed with supportive medications and good nursing care. It is very important to know that the veterinarians providing your Westie's chemotherapy treatment are experienced in treating cancer with chemotherapy drugs. They will closely monitor your Westie during treatment and perform frequent bloodwork to ensure the chemotherapy is not causing significant damage to the bone marrow cells.

Radiation therapy can also be used to slow growth of your Westie's bladder tumor for a period of time. Radiation therapy uses a high-energy X-ray beam to target and kill cancer cells. This type of radiation is non-painful and does not pose any risk of radiation exposure to owners after treatment has been performed. Radiation therapy is performed with the dog under short-term general anesthesia to make sure there's no movement while the treatment is being delivered. Similar to chemotherapy, radiation therapy tends to be well-tolerated. Side effects of radiation therapy can include hair loss over the radiation site and temporary inflammation of the colon (which can cause diarrhea) and bladder (which can cause transient worsening of the urinary symptoms). More recently, veterinary oncologists have been utilizing radiation therapy in combination with chemotherapy to most effectively treat bladder cancer in dogs.

The outlook ("prognosis") for dogs with bladder cancer is guarded and depends a great deal on:

- Initial size and location of the tumor
- Amount of invasion of the bladder wall and surrounding tissues in the abdomen
- Metastasis (spread) of tumor cells to lymph nodes and other organs in the body
- Response of tumor cells to chemotherapy and/or radiation therapy

According to Dr. Deborah Knapp, et al, the median survival of all breeds of dogs with the early stages of transitional cell carcinoma, when treated with chemotherapy, is 218 days. For dogs with more advanced disease, the survival is about half of that interval. Of course, the outcome for any individual dog is hard to predict, but transitional cell carcinoma of the urinary bladder is one of the most serious health problems

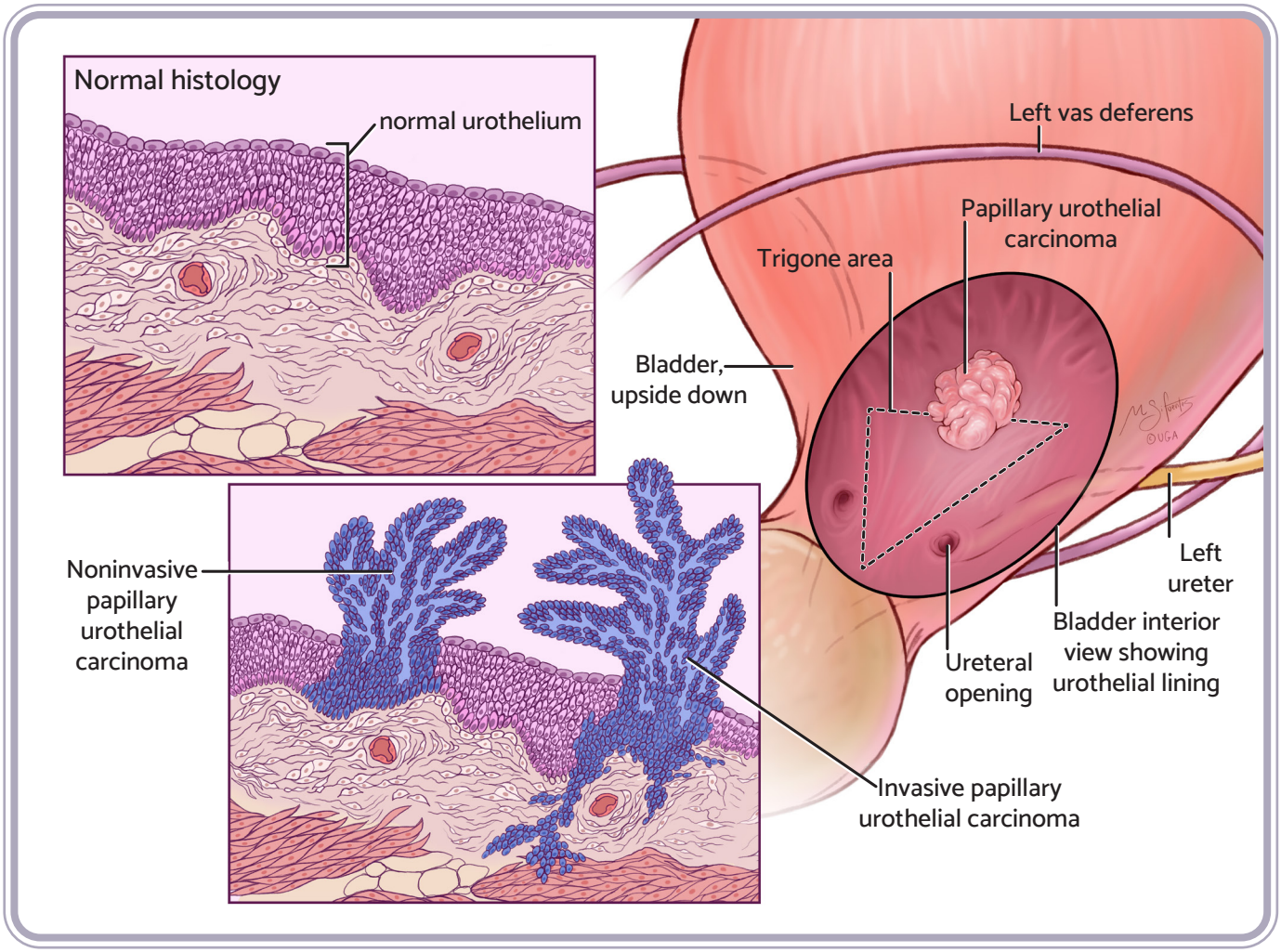

Figure 9.5 - Depiction of papillary urothelial carcinoma in the trigone area of the bladder.

affecting Westies and other short legged Scots breed terriers (see below).

The early detection of bladder cancer in "high risk" dogs (including Scottish and West Highland White Terriers, Shetland Sheepdogs, among others) would allow more timely intervention (chemotherapy, radiation therapy, etc.) and is likely to be associated with a better prognosis. Ultimately, your veterinarian's goal is to help maintain your Westie's quality of life and minimize any side effects of the treatment. Chemotherapy and radiation treatment may not be the right decision for every Westie and every owner. You need to discuss this with your veterinarian when deciding if and how to treat your dog. Most veterinarians will also discuss the use of medications to control any discomfort and will be candid about the probability of the treatments being effective. If you decide that chemotherapy or radiation therapy is not the best treatment option for your Westie, then your veterinarian will discuss other palliative (i.e., hospice) treatment options to help keep your Westie comfortable.

Frontiers in Cancer Diagnosis and Treatment

There is growing interest in the development of better screening tests for cancer in dogs. The goal of these tests is either to identify the presence of cancer before the dog starts to show any symptoms, or to help clarify whether a dog's symptoms could be caused by cancer rather than some other disease. With early detection of cancer, we can start treatment sooner and potentially improve outcomes for our dogs. This concept is similar to how physicians recommend cancer screening tests for different conditions in people, including mammograms to look for breast cancer or colonoscopies to look for colon cancer.

These cancer screening tests are also called "liquid biopsy" tests. There are various "liquid biopsy" tests available through different companies, including the "IDEXX Nu.Q Canine Cancer Screen" and the PetDx "OncoK9 ®" test. Most of these "liquid biopsy" tests analyze blood samples for the presence of certain types of DNA or other circulating molecules that are associated with cancer. A positive test suggests that your dog could have cancer. However, the results of these tests should be interpreted with caution by your veterinarian.

The sensitivity and specificity of these tests can be highly variable, meaning that there is a risk of a false positive or false negative result. For example, your Westie might have a positive test result even if they do not actually have cancer (i.e., a false positive). Conversely, your Westie's test result could be negative, but they could still have undetected cancer (i.e., a false negative). Another consideration with these tests is that a positive result does not indicate the specific type of cancer. With a positive result, your veterinarian will likely recommend additional testing like full bloodwork and imaging (i.e., chest x-rays and abdominal ultrasound) to look for cancer in your Westie's body. Your veterinarian may still recommend these diagnostic tests if they are highly suspicious of cancer, even if the "liquid biopsy" result is negative. As time goes on, the overall quality of these "liquid biopsy" tests are likely to improve, increasing the utility of these tests as a means for your veterinarian to screen your Westie for cancer.

Another exciting area of growth in the veterinary cancer field is the use of "precision medicine". With this approach, the treatment plan for an individual dog's cancer is determined based on analysis of the unique genetics of their tumor, rather than taking a "one-size-fits-all" approach. There are several companies (e.g., FidoCure ® and Vidium Animal Health ®) that offer precision medicine tests for cancer in dogs. To submit these tests, your veterinarian first needs to obtain a biopsy or fine needle aspirate sample of your Westie's tumor. The sample then gets submitted to the company so they can perform full genetic sequencing of the DNA of the tumor.

Your dog's tumor DNA then is screened for certain genetic mutations that occur commonly in cancer. If one or more of these mutations are identified, then the test will make recommendations for certain medications that can be used to target the mutation (called "targeted therapy"). These "targeted therapy" drugs work through different mechanisms, including activation of a dog's own immune system to fight the cancer cells or by preventing blood flow to the tumor.

Theoretically, using "targeted therapy" drugs specific to an individual dog's cancer might treat their cancer more effectively than conventional chemotherapy or radiation therapy. However, the true efficacy of these treatment is not yet proven, and more research is needed to determine which types of cancer might be most responsive to "targeted therapy". If your Westie is diagnosed with cancer, it would be most prudent to discuss all treatment options, including conventional and "precision medicine" approaches, with your veterinarian and a veterinary oncologist.

In summary

We collectively (owners, breeders, veterinarians, and research scientists) need to put forth our best efforts to identify the causes and to find effective treatments for tumors in our dogs.

We owe them that.

Acknowledgements

Megan Reeves Sifuentes, a medical illustrator in Educational Resources of the College of Veterinary Medicine at the University of Georgia, created the illustrations used in this chapter.

Relevant References

Allen, DK, Waters, DJ, Knapp, DW, "High urine concentrations of basic fibroblast growth factor in dogs with bladder cancer," J Vet Intern Med 1996; 10:231-23

Backer, LC, Coss, AM, Wolkin, AF, Flanders, WD, Reif, JS, "Evaluation of associations between lifetime exposure to drinking water disinfection by-products and bladder cancer in dogs," J Am Vet Med Assoc 2008; 232:1663–1668

Borjesson, DL, Christopher, MM, Ling ,GV," Detection of canine transitional cell carcinoma using a bladder tumor antigen urine dipstick test," Vet Clin Pathol 1999; 28:33-38

Bracha, S, McNamara, M, Hilgart, I, Milovancev, M, et al, "A multiplex biomarker approach for the diagnosis of transitional cell carcinoma from canine urine," Analytical Biochem 2014; 455: 41–47

Decker, B, Parker, HG, Dhawan, D, Kwon, EM, 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

Fulkerson, CAM, Knapp, DW, "Management of transitional cell carcinoma of the urinary bladder in dogs: A review," Vet J 2015; 205: 217–225

Glickman, LT, Raghavan, M, Knapp, DW, Bonney, PL, Dawson, MH, "Herbicide exposure and the risk of transitional cell carcinoma of the urinary bladder in Scottish Terriers," JAVMA 2004; 24: 1290-1297

Grossman, HB, Messing, E, Soloway, M, et al, "Detection of bladder cancer using a point-of-care proteomic assay," JAMA 2005; 293: 810-816

Hajdinjak, T, "UroVysion FISH test for detecting urothelial cancers: meta-analysis of diagnostic accuracy and comparison with urinary cytology testing," Urol Onco 2008; 26: 646-651

Hanazono, K, Fukumoto, S, Endo, Y, Ueno, H, Kadosawa, T, Wano, Uchide, T, "Ultrasonographic findings related to prognosis in canine transitional cell carcinoma," Vet Radiol Ultrasound 2014; 55: 79–84

Irani, J, Desgrandchamps, R, Millet, C, et al, "BTA stat and BTA TRAK: a comparative evaluation of urine testing for diagnosis of transitional cell carcinoma of the bladder," Eur Urol 1999; 35: 89-92

Knapp, DW, Henry, CJ, Widmer, WR, Tan, KM, et al,, "Randomized trial of cisplatin versus firocoxib versus cisplatin/firocoxib in dogs with transitional cell carcinoma of the urinary bladder," J Vet Intern Med 2013; 27:126–133

Knapp DW, McMillan SK (2001). Tumors of the Urinary System. In Withrow, SJ and MacEwen, EG (Eds), Small Animal Clinical Oncology, 3rd ed. WB Saunders Co, Philadelphia, PA.

Knapp, DW, Peer, WA, Conteh, A, Diggs, AR, et al, "Detection of herbicides in the urine of pet dogs following home lawn chemical application," Sci Total Environ 2013; 456–457: 34–41

Knapp, DW, Ramos-Vara, JA, Moore, GE, Dhawan, D, et al, "Urinary bladder cancer in dogs, a naturally occurring model for cancer biology and drug development," ILAR Journal 2014; 55: 100-118

Luethcke KR, Ekena J, Chun R, Trepanier LA. Glutathione S-transferase theta genotypes and environmental exposures in the risk of canine transitional cell carcinoma. J Vet Intern Med. 2019;33(3):1414–1422.

McMillan, SK, Boria, P, Moore, GE, Widmer, WR, Bonney, PL, Knapp, DW, "Antitumor effects of deracoxib treatment in 26 dogs with transitional cell carcinoma of the urinary bladder," JAVMA 2011; 239:1084–1089

Messing EM, Madeb R, Young T, et al, "Long-term outcome of hematuria home screening for bladder cancer in men," Cancer 2006; 107: 2173-2179

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.

Mochizuki, H, Shapiro, SG, Breen, M, "Detection of copy number imbalance in canine urothelial carcinoma with droplet digital polymerase chain reaction," Vet Pathol 2016; 54(4): 764-72

Norris, AM, Laing, EJ, Valli, VE, Withrow, SJ, et al, "Canine bladder and urethral tumors: A retrospective study of 115 Cases (1980-1985)," J Vet Int Med 1992; 6:145-153

Robat, C, Burton, J, Thamm, D, Vail, D, "Retrospective evaluation of doxorubicin–piroxicam combination for the treatment of transitional cell carcinoma in dogs," J Small Animal Practice 2013; 54, 67–74

Smith, N, Luethcke K, Craun K, Trepanier L, "Risk of bladder cancer and lymphoma in dogsis associated with pollution indices by county of residence," Vet Comp Oncol 2022; 20(1): 246-255