



PURINA Pro Club

Boxer Update

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Hemangiosarcoma Research Focuses on Growth Signaling Pathways

Hemangiosarcoma has become one of the most feared cancers in Boxers. Besides being increasingly common, it usually develops unnoticed with a dog showing few or no signs until the cancer progresses to the final stages.

At this year's American Boxer Club National Specialty held in May at Fort Mitchell, Ky., the Charitable Trust Foundation presented a slide show featuring photographs of notable Boxers that had recently died. One after another had died from cancer, and among them were dogs that had died from hemangiosarcoma.

Bravo Boxers breeder Susan Finley of Crestwood, Ky., who lost a Boxer to hemangiosarcoma several years ago, says, "These were some of the finest dogs in the breed, with the best veterinary care. It was terribly sad to see cancer listed as the cause of death for so many. Cancer was far and away the biggest category."

Researchers across the country are working to learn more about the causes of canine cancer. Hemangiosarcoma is particularly challenging because it is an aggressive cancer that usually has metastasized, or spread, by the time it is diagnosed. This cancer comes from endothelial cells that line the blood vessels. As a result, the

tumor has a constant blood supply and access to blood vessels, which helps to facilitate its spread throughout the body.

The good news for owners and breeders of Boxers is that researchers are making steady progress in the research of hemangiosarcoma. A

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recently completed study at the Oregon Cancer Center for Animals (ORCCA), located at Oregon State University, tested a new class of drugs, tyrosine kinase inhibitors, to determine their effectiveness in stopping cancer cell growth. Though the work is in the early stages, Stuart Helfand, D.V.M., professor of oncology and director of oncology services, is optimistic that

drugs that interrupt growth signaling pathways may one day show promise in treating hemangiosarcoma.

Meanwhile, Jaime Modiano, V.M.D., Ph.D., the recently appointed Perlman Professor of Comparative Oncology at the University of Minnesota, led research that resulted in a blood test to detect hemangiosarcoma when the cancer is in its early stages and thus when dogs have a greater chance of receiving effective therapy. The research continues to determine how early the blood test can detect disease and how to pinpoint cancer cells for effective therapy.

Modiano developed the blood test while he worked at the University of Colorado at Denver and Health Sciences Center.

A Prevalent Cancer in Dogs

"Hemangiosarcoma is a silent killer," says Finley. "When my 7-year-old bitch, 'Abbie,' developed hemangiosarcoma, the only indication something may be wrong was that she started slowing down a bit and gaining weight through her middle. I attributed it to the aging process."

Abbie, formally known as Bravo's Abnecki Maiden, had competed in obedience and earned a Companion Dog title.

Unconcerned, Finley and her husband went on a Caribbean vacation and left Abbie with Finley's mother. "When my mom called to say that Abbie wasn't eating, we weren't too worried," she says. "Her appetite didn't come back the next day, so my brother-in-law took Abbie to the veterinarian. Our vacation ended immediately when tests revealed a large mass on her spleen."

Abbie had surgery the next day to remove the spleen and tumor mass, but she died six weeks later. A second surgery had revealed large and small metastasized hemorrhaging tumors, the definitive signs of hemangiosarcoma.

Hemangiosarcoma most often originates in the spleen. In time, the tumor

Recognizing Signs of Hemangiosarcoma

Hemangiosarcoma is often called the "silent cancer" because it develops slowly and is essentially painless. Signs of this lethal cancer are frequently not evident until the advanced stages when the tumor is resistant to treatment.

Owners should watch for signs of hemangiosarcoma and report them right away to their veterinarian. Signs of hemangiosarcoma include:

- Intermittent fatigue;
- Weight loss or lack of appetite;
- Pale gums;
- Unusual bleeding;
- Rapid pulse;
- Fast breathing or panting;
- Sudden or unexpected weakness;
- Waxing and waning weakness;
- Development of lumps or tumors; and
- Depression.

Hemangiosarcoma Research

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ruptures, showering tumor cells throughout the abdomen where they implant and grow. Many dogs die from acute internal hemorrhaging secondary to the tumor rupturing or from the rupture of the tumor near or in a critical area.

Veterinarians primarily see hemangiosarcoma in the spleen, liver, skin and heart. Other less common primary sites are the kidneys, mouth, muscle, bone, brain, urinary bladder, and peritoneum, a large membrane in the abdominal cavity that lines the abdominal cavity and organs. Though tumors can become larger than a grapefruit, sometimes it's not possible to feel the tumor during palpation. The most common sites of metastases are the lungs and liver, yet in dogs with multiple tumors, it may be difficult to determine the primary tumor site.

Hemangiosarcoma occurs more often in dogs than any other species and represents about 7 percent of all canine cancers. The prevalence in Boxers is not known exactly. Other breeds at risk are German Shepherd Dog, Golden Retriever, Great Dane, English Setter, Pointer, and Sky Terrier. The cancer is most commonly seen in male dogs between 8 and 10 years of age, although it also is seen in young dogs.

Though she has no evidence, Finley believes more Boxers die from hemangiosarcoma than is realized. "The cancer gets diagnosed in show dogs and working dogs because their owners are aware of the problem and motivated to track their dogs' health problems," she says. "Since these dogs are groomed or inspected frequently, their owners are likely to notice small changes. They also are likely to take their dog to the veterinarian as soon as they see or feel something unusual, and are more likely to follow up on the diagnosis."

Signs of hemangiosarcoma are subtle. Once the cancer has spread, a dog may show physical weakness, a distended abdomen, rapid pulse, fast breathing or panting, weight loss, pale gums, and anemia. Lethargy, depression and lack of appetite are common. Owners, such as Finley, may sense that something isn't quite right with their dog but be unable to detect the problem.

Early signs of the cancer may be intermittent. A dog's breathing may become labored because internal bleeding reduces the oxygen content in the bloodstream. However, if the bleeding stops and the dog reabsorbs blood from the abdomen, a process called autotransfusion, a dog may appear normal. In addition, lethargy may resolve, and appetite may improve.

Learning More About Cancer

To learn more about the treatment of hemangiosarcoma and other canine cancers, you may visit the following Web sites:

- The Encyclopedia of Canine Veterinary Medical Information at www.vetinfo.com/dencyclopedia/dehemsarcoma.html.
- The Modiano laboratory at the University of Minnesota at www.modiano.lab.org/cancer/cancer_hemangiosarcoma.shtml.
- The University of Georgia College of Veterinary Medicine at www.vet.uga.edu/VPP/clerk/frankhauser/index.php.
- The Perseus Foundation at www.perseusfoundation.org.

If hemangiosarcoma is discovered early, when the tumor is easiest to treat with surgery and chemotherapy, a dog may survive seven to eight months. After surgery to remove a tumor, a dog can leave the hospital two days later, tail wagging and feeling great, but the tumor will regrow in two to four months, Helfand says. Without treatment, life expectancy is about two months.

The 'Lock-and-Key' Approach

At the Oregon Cancer Center for Animals, which opened two years ago, Helfand directs research that concentrates on a "lock-and-key" approach to understanding cancer. "A 'lock' is a protein, or a receptor on a cell that is specific to the cell's function, and the 'keys' that fit the lock are growth factors that stimulate endothelial cells and bind the receptors, or locks," he explains.

"Cancer is a disease in which bad cells grow rapidly, and sometimes a lock may mutate and switch on without the need to receive signals from an external key," Helfand says. "As we learn more about these lock-and-key interactions, we may be able to better understand the behavior of hemangiosarcoma and other cancers."

"If we can shut down the cancer pathway when the key is in the lock, we may be able to block normal internal signaling that triggers the cell nucleus to divide. If we could prevent the key from going into the lock or disrupt the downstream proliferation signals, we could potentially block cancer growth."

Results of the recently completed hemangiosarcoma study, funded by the Morris Animal Foundation, have yet to be published in a scientific journal so Helfand can share limited information about the findings.

"We feel comfortable reporting there are potential targets, or so-called locks in the lock-and-key analogy, that are worth pursuing," Helfand says. "Our work concentrated first on determining whether the locks exist and then determining whether it is possible to successfully block the cancer pathways in order to arrest cell growth."

"Finding drugs that interfere with these pathways that are well tolerated

in dogs will be a challenge but is something that potentially can be addressed in future research. The important thing is that we can use the lock-and-key strategy to find more effective treatments for hemangiosarcoma as well as other canine cancers.

"I believe it is just a matter of time, which partly is dependent on additional funding, before we learn how to adapt growth factor blockers so they can effectively help dogs diagnosed with hemangiosarcoma."

In the meantime, until an effective therapy is discovered for Boxers diagnosed with hemangiosarcoma, breeders and owners should pay attention for subtle signs of this life-threatening cancer. The sooner the cancer is diagnosed and treatment can begin, the more likely a dog will live longer. ■

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