



Lymphoma: Death be not proud

Signs and
treatment of
this common
cancer

By Leslie Crane Rugg
and Eva Saks

Lymphoma terrifies dog owners—and rightly so. Mona Rosenberg, DVM, chief oncologist of Veterinary Cancer Group at the City of Angels Veterinary Specialty Center, says without treatment, typical survival time is four weeks. Even with treatment, this cancer of the blood kills quickly. Nonetheless, Jaime Modiano, VMD, professor of oncology and comparative medicine at the University of Minnesota's veterinary school and Masonic Cancer Center, says progress is happening. "Lymphoma may become a manageable disease," he says, "maybe even in the next decade."

Ted Valli, DVM, diplomate at the American College of Veterinary Pathologists, says lymphoma (lymphosarcoma) describes more than 30 cancers of the lymphocytes (white blood cells) and lymphatic system. Normally, lymphocytes fight infection; they are "the main effector cells of the immune system. The cancer develops because the lymphocytes are reproducing too rapidly or not dying rapidly enough," Michael Childress, DVM, assistant professor of oncology at Purdue University's School of Veterinary Medicine, says. Excessive lymphocytes cause

tumors and disable healthy cells, leading to organ failure and death. The disease affects lymph tissue as well as non-lymphoid organs (spleen, bone marrow) and therefore can occur throughout the body.

One in 15 dogs contracts lymphoma, making it the most common life-threatening cancer, Modiano says. Lymphoma affects some breeds more dramatically than others, says Matthew Breen, Ph.D., professor of genomics at North Carolina State University's College of Veterinary Medicine. It strikes one in four Boxers and one in eight Golden Retrievers. Rosenberg also sees it frequently in Labradors, Saint Bernards, Basset Hounds, Scottish Terriers, Rottweilers, German Shepherd Dogs, and Vizslas.

Causes and Symptoms

Lymphoma's cause is unknown. Valli says, "In general [it] is a disease of aging, with any persistent focus of inflammation a risk factor." Various factors probably contribute to all cancers; Rosenberg lists "the aging process, genetics, the environment we live in, a deterioration of the immune system, and just plain bad luck."

She continues, "Genetics plays an important role. Now that the canine genome has been identified, several research labs are searching for genetic abnormalities and mutations that may be in part responsible for the development of lymphoma. Viral involvement has been hypothesized but never confirmed as a risk factor."

Although Rosenberg says that "environmental factors have not been definitively identified," Jean Dodds, DVM, Hemolife founder, says that "environmental exposures are definitely of concern." Carcinogens lurk in everything from weed killers (herbicides)—in particular, formula 2,4,5-T, and formula 2,4-D, also known as the active ingredient in Agent Orange—to grooming products to food preservatives to plastics.

Veterinary attention should be sought immediately upon discovering symptoms of any of the four types of lymphoma:

- **Multicentric** (most common) forms in the lymph nodes. Note swelling in the neck, front legs, or groin.
- **Gastrointestinal/alimentary** forms in the digestive tract. Symptoms include vomiting, diarrhea, and lack of appetite.
- **Mediastinal** forms in the thymus gland, impairing lung and/or heart function. Affected dogs might show shortness of breath, post-meal vomiting, or abnormal heartbeat.
- **Extranodal** (very rare) usually affects skin and mucus membranes, which are non-lymphoid tissues. Note ulcerations and scratching.

Lymphoma is confirmed by a positive biopsy. A veterinary oncologist will then "stage" the cancer, determining its extent and nature, usually through some combination of blood panels, bone-marrow aspirates, X-rays, and ultrasound. The prognosis is worst for stage five, when disease has spread throughout the body, including bone marrow.

Treatment Options

Because most lymphomas are disseminated rather than focal (encapsulated) cancers, they cannot be treated by radiation or surgery. The standard of care is the CHOP (or Wisconsin) protocol, a chemotherapy regimen that combines four drugs: Cyclophosphamide (C), Doxorubicin (H),

Vincristine (O), and Prednisone (P). CHOP causes remission in 85 percent of dogs. "It is rare to have a dog with lymphoma that is not a good candidate [for CHOP]," Rosenberg says. "Even the dogs with advanced disease deserve a chance." Unlike people, most dogs suffer few side effects from chemotherapy, other than gastrointestinal upset. Few breeds experience hair loss. Unfortunately, the average remission lasts only 14 months. Incidentally, Rosenberg tailors CHOP specifically for dogs with the multi-drug resistance gene mutation (MDR-1) who sometimes face difficulties with Vincristine and Doxorubicin.

If a dog owner decides against chemotherapy, there are few other options. Some veterinarians may suggest Prednisone, which induces remission in 20 to 50 percent of dogs, Childress says. However, he points out that Prednisone alone possibly precludes a later switch to more aggressive treatment, as North Carolina State University studies suggest that Prednisone may induce resistance to CHOP.

Nicole Schiff, DVM/CVA, performs acupuncture on dogs with lymphoma. "Depending on where the lymphoma is, acupuncture can be quite helpful in relieving unpleasant symptoms both from their illness as well as from chemotherapy," she says. She cites nausea and diarrhea as examples of what acupuncture can treat.

Whether diet is intrinsic to cancer treatment or palliative at best remains controversial. Modiano downplays the role of food, asserting that the only verified nutrition/cancer link is the danger of "overnutrition" (eating too much). "We know obesity leads to deterioration in the immune system, so this is important," Rosenberg says.

Director of Angel Care Cancer Center Gregory Ogilvie, DVM, DACVIM (internal medicine, oncology), DECVIM-CA (oncology), points out published data confirming that "nutrition is linked to an increased risk of developing as much as 30 percent of cancer in people and thus, appropriate nutrition may have a huge impact." Ogilvie continues pioneering work in nutrition he began as director of the Medical Oncology Research

Laboratory of the Animal Cancer Center at Colorado State University. He recommends his cancer patients eat a diet of "relatively low amounts of simple carbohydrates, moderate quantities of high-quality proteins, increased amounts of omega-3 fatty acids ... and relatively low amounts of omega-6 fatty acids."

On the Horizon

Lymphoma research is widespread, supported by public entities like the National Cancer Institute's Comparative Oncology Trials Consortium and private organizations like the AKC Canine Health Foundation. Hopeful directions include:

- **Targeted therapy**, which improves chemotherapy delivery systems, allowing drugs to attack only lymphoma cells and spare normal cells, thereby permitting stronger drugs to be used.
- **Anti-angiogenic therapy**, which starves tumors by destroying blood vessels that supply tumor nourishment.
- **Immunotherapy**, which harnesses the body's own immune system to destroy cancer. Michael Lawman, Ph.D., director of Basic Research Pediatric Hematology/Oncology at St. Joseph's Children's Hospital in Tampa, Florida, has developed a canine lymphoma vaccine, in collaboration with Morphogenesis, Inc. Lawman points out that his vaccine doesn't immunize healthy dogs against lymphoma but rather provides a way to extend a stricken dog's life span.
- **Induced apoptosis**, which precipitates programmed cell death in cancer cells.
- **Refined classification**, designed by Valli and based on the World Health Organization system for human disease, to enhance diagnostic accuracy and fine-tune treatment depending on lymphoma subtype.

For owners of dogs affected with lymphoma, the excruciating treatment decision is deeply personal. One thing is clear: Cherish your dog and enjoy quality time, whatever you choose. **GZ**

Leslie Crane Rugg and Eva Saks collaborate on print and media projects related to dogs and culture. They dedicate this article to Brome and Bruce, their beloved dogs lost to cancer.