



# Lymphoma in Dogs

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Lymphoma, also known as lymphosarcoma, is a common cancer of lymphocytes, which are a specific type of white blood cell in the immune system. The cancer is often aggressive and has a high mortality rate. Lymphoma is a rapidly-growing cancer that is able to advance anywhere where there is lymph tissue, which includes nearly every organ in the body. Although there are breeds that appear to be at increased risk for this disease, lymphoma can affect any dog of any breed at any age. The cancer is most commonly located in lymph nodes, bone marrow, liver and/or spleen, but it can occur in almost any tissue of the body. Lymphoma is similar to non-Hodgkin's lymphoma in human patients.

There are 2 forms of lymphocytes: B and T cells. Lymphoma may develop from either type of lymphocyte, but B-cell is more common in dogs and is associated with a better response to treatment.

## Symptoms and Types

The symptoms of lymphoma are variable and depend upon where the cancer is located and how advanced it is. Enlarged lymph nodes or "glands" are the most common symptom of lymphoma. Dogs still may feel normal at this point in the disease or they may have vague symptoms.

Nonspecific signs may include:

- Distended abdomen
- Lethargy
- Coughing
- Shortness of breath
- Fever
- Poor appetite
- Increased thirst
- Vomiting and/or diarrhea
- Weight loss
- Bruised skin or open wounds

Multicentric lymphoma refers to lymphoma within multiple lymph nodes and other organs, and it is the most common form of lymphoma in dogs. Multicentric lymphoma accounts for approximately 80% of all lymphoma cases. However, localized forms of lymphoma can also occur in dogs, including lymphoma of the central nervous system, chest, skin and gastrointestinal (digestive) tract. Lymphoma can also be localized to the eyes, kidneys, liver and bone.

Multicentric lymphoma is often first detected as painless but enlarged lymph nodes present under the skin. Common locations include under the jaw, in front of the shoulders, the armpits, the groin area or behind the knees. Lymphoma can affect lymph nodes that are not visible or palpable from outside the body, such as those inside the chest or in the abdomen. The abdomen may be distended. This is the most common form of lymphoma in dogs, and generally the most easily diagnosed form.

Lymphoma of the central nervous system (CNS lymphoma) is very uncommon and typically causes behavior changes, lack of coordination, seizures and blindness.

Lymphoma in the chest cavity (mediastinal lymphoma) occurs in the thymus gland and causes coughing and labored breathing. Symptoms may mimic congestive heart failure.

Lymphoma of the skin (cutaneous lymphoma or mycosis fungoides) initially appears as hair loss and redness of the skin, often surrounding the eyes and lips. It will advance to include other areas of skin, and lesions may vary from crusting to lumps to bruising or raw ulceration. The skin may be itchy or painful, and skin biopsies are needed to confirm a diagnosis.

Lymphoma of the gastrointestinal tract (alimentary lymphoma) may develop at any area of the digestive tract, including the stomach, small intestine, large intestine and/or rectum. Signs of gastrointestinal lymphoma include vomiting, diarrhea, weight loss, lethargy, loss of appetite and diarrhea.

Lymphoma generally does not cause pain unless the lymph node swelling is severe or the cancer is invading into bone.

### Causes

The cause of lymphoma is unknown. Dogs with higher exposure to 2,4-D herbicides used for lawn care seem to have a slightly higher incidence of lymphoma. Certain breeds are disproportionately affected, suggesting a genetic component to this disease. A random genetic mutation or other abnormal chromosomal recombination event is suspected in most cases of lymphoma.

### Diagnosis

The initial evaluation for a dog with nonspecific symptoms of illness first involves a thorough physical examination and a complete history.

The most common way to diagnose lymphoma in dogs is to collect samples from enlarged lymph nodes or other affected organs. A fine needle aspirate (FNA) involves inserting a small needle into the suspicious lymph nodes, then withdrawing fluid and cells. The sample is examined under a microscope by a pathologist. This process, called cytology, is often diagnostic for lymphoma.

If FNA and cytology are inconclusive, biopsies of one or more enlarged lymph nodes are needed. A biopsy collects pieces of tissue, rather than only cells. A lymph node biopsy typically requires a local anesthetic to collect a core sample. Suspicious lymph nodes may be entirely removed under general anesthesia for more thorough examination.

Routine blood work and a urinalysis are also typically performed to check for low red blood cell numbers (anemia), immature white blood cells in the blood stream, increased calcium and liver enzyme levels. Urine testing may reveal a concurrent bladder infection. Advanced diagnostic tests include immunocytochemistry, immunohistochemistry, flow cytometry and PCR (polymerase chain reaction) to determine whether lymphoma is B-cell or T-cell.

Other diagnostic tests may be useful to determine the extent of lymphoma throughout the body. Chest radiographs (X-rays) and ultrasound examinations can identify enlarged lymph nodes and other organs, as well as other isolated masses. Bone marrow aspiration can evaluate abnormal cell counts, and cerebrospinal fluid (CSF) tap is useful if the dog is showing neurological signs. Endoscopy or surgery to biopsy the gastrointestinal tract may be necessary.

### Staging

The stages of lymphoma in dogs basically are as follows:

- Stage 1: Only one lymph node is involved
- Stage 2: Multiple lymph nodes on one side of the diaphragm are involved
- Stage 3: Multiple lymph nodes on both sides of the diaphragm are involved
- Stage 4: Liver and/or spleen involvement, with or without enlarged lymph nodes
- Stage 5: Involvement of bone marrow, blood or any other organ  
(Stage 3 and Stage 4 are the most common stages for dogs)

Each stage can further be classified:

- Substage A: No signs of illness
- Substage B: Concurrent signs of illness, such as loss of appetite, lethargy, weight loss, etc.

Patients who are initially Substage A will eventually develop signs of illness and become Substage B. Patients treated in Substage A have a much better chance for long term survival.

### Treatment

The goal of lymphoma treatment is to achieve complete remission of the cancer and thereby restore the patient's normal quality of life for as long as possible. Remission is defined as complete or partial disappearance of the signs and symptoms of cancer in response to treatment. Remission of lymphoma

does not mean a cure, since a few microscopic cells may remain and the cancer may ultimately recur (relapse).

Lymphoma in dogs is usually a generalized or systemic disease, which requires treatment throughout different systems of the body. Chemotherapy, which simply means the use of drugs to treat cancer, is the standard of care for lymphoma. More than 75% of dogs with lymphoma will achieve a complete remission with chemotherapy. Chemotherapy may be administered as oral tablets or capsules, as well as injections. The most successful therapy for lymphoma includes combinations of different chemotherapy medications, compared to single drugs. Chemotherapy protocols typically contain from 3-5 different chemotherapy drugs, each of which affects cancer cells in a different way. If some of the cancer cells are resistant to one drug, ideally they will be sensitive to another drug in the protocol. The sooner that a multiple-drug therapy is started, generally the better the chance of favorable outcome. Most lymphoma chemotherapy protocols include weekly treatments for 6 to 8 weeks before decreasing the frequency of treatment. Common chemotherapy drugs for lymphoma include vincristine, cyclophosphamide, L-asparaginase and doxorubicin. Other drugs include epirubicin, lomustine, and mitoxantrone, and treatment protocols may include other less-commonly used agents.

Prednisone is the most basic and cost-effective treatment of lymphoma, although life expectancy is significantly shorter and side effects may be more evident. If prednisone is used for a significant period of time before introducing chemotherapy medications, the chemotherapy is often less effective.

It is important to realize that decades of research have gone into patient comfort, minimizing side effects and maximizing response with chemotherapy for lymphoma. Chemotherapy may cause side effects in certain patients, although dogs generally tolerate chemotherapy treatments without the severe side effects that can affect human patients. Clear communication between the treating veterinarian and the patient's family is essential, along with close monitoring for changes at home as well as blood cell counts at the time of each treatment. In case of serious complications, treatment should be decreased or stopped altogether.

When lymphoma relapses (recurs), treatment is attempted by reintroducing the original chemotherapy medications that were initially successful. For most patients, the second response is approximately half of the duration seen in the initial therapy. Some animals certainly enjoy long-term second remission, especially if the patient had good response in the first therapy. If reinduction fails, the use of "rescue" agents or protocols can be attempted. These include drugs that are not found in the standard chemotherapy protocol. They are kept in reserve for later use.

Radiation therapy may be combined with chemotherapy, although research to date has not shown a clear improvement in the success of remission or life expectancy for dogs with lymphoma. Stem cell transplant (SCT) is another possible treatment option with a substantially improved prognosis. SCT cannot be performed on all dogs with lymphoma. Currently, the protocol requires that dogs be in either complete remission or very close to complete remission before they can undergo bone marrow transplant treatment. Therefore, they need to be treated first with chemotherapy. Not all patients are candidates for SCT due to concurrent health concerns, and the treatment costs are considerable.

Treatment is not recommended for female dogs during pregnancy.

Chemotherapy is also potentially hazardous for people, and you should talk to the treating veterinarian about safe handling of chemotherapy medications at home. Basic precautions include wearing gloves when administering medications or cleaning up urine or bowel movements.

### **Outcome**

Canine lymphoma usually responds well to chemotherapy treatment. Frequent examinations and blood tests are necessary to evaluate the success of treatment and to ensure that treatments are not negatively affecting the patient. Side effects may include digestive tract upset or fatigue, but these effects are transient and typically mild. Hair loss may occur in certain breeds including the poodle, shih tzu, lhasa apso, maltese, Bichon Frise and Old English sheepdog.

The life expectancy of untreated dogs with lymphoma is about 4 to 6 weeks after diagnosis. The cancer will infiltrate an organ to such an extent that organ fails. Appetite declines, breathing becomes more labored, and the patient weakens and dies.

Dogs that respond to chemotherapy and achieve complete remission remain free of symptoms and return to normal lifestyle. A patient in complete remission will appear to be free from cancer. In dogs that undergo chemotherapy, life expectancy can be extended to a year on average and often longer. One year can be almost 10 percent of a dog's expected life span, so the remission rate and increased life expectancy with lymphoma treatment is often well worth it when the quality of life remains good. As many as 25% of dogs are long-term survivors (longer than 2 years). Unfortunately, lymphoma is almost always progressive and ultimately fatal. At some point lymphoma becomes resistant to therapy and no further remissions can be obtained. Treatment of lymphoma rarely cures the disease although multiple remissions may be possible. The goal of treatment is to make the patient feel better and live longer, with a very good quality of life.

### **A special note about Indolent Lymphoma**

Indolent lymphoma is a less common slow growing form of lymphoma, compared to lymphoblastic or high grade lymphoma. In general, dogs with indolent lymphoma will be middle-age to older and have no clinical signs of illness associated with their lymphoma. Early stages of indolent lymphoma may last many months and have low response to treatment. Diagnosis of indolent lymphoma usually requires biopsy of an enlarged lymph node. Life expectancy for dogs with indolent lymphoma is often 2 years or longer. Left untreated, indolent lymphoma may not affect quality of life or survival time. However, many cases of indolent lymphomas in late stages of progression will eventually behave like the more common high-grade lymphoma.

*Please note that this information does not replace a direct consultation, with the patient and all clinical data, with a board-certified veterinary oncologist. To schedule an appointment with Dr. Sue Downing at Animal Specialty & Emergency Center, please call (310)473-5906.*

### **Other Resources**

- [Modiano Lab \(University of Minnesota\)](#) is geared to finding the causes for cancer, understanding the mechanisms that drive tumor behavior and tumor progression, and ultimately identifying the targets that will allow us to prevent, control, and treat different types of cancer.
- [North Carolina State University's College of Veterinary Medicine](#) was the first veterinary program in the nation to offer canine stem cell transplants for lymphoma in a clinical setting.
- Veterinary Cancer Society has a [searchable clinical trials database](#) that you may access to see if there is a trial that may be of benefit for your pet.

