



## Canine Lymphoma

Lymphoma (lymphosarcoma) is one of the most commonly diagnosed cancers in dogs. It is a cancer of lymphocytes (a type of blood cell) and lymphoid tissues. Lymphoma can be located in lymph nodes, liver, spleen, intestinal tract, skin (cutaneous) and the bone marrow.

Dogs with lymphoma are mostly commonly between 6-9 years of age, but any age can be affected. Unfortunately, we do not know the cause of this disease, although there are some studies that suggest a genetic component in certain breeds such as Boxers, Golden Retrievers, German Shepherds, Scotties, Westies and Pointers.

Staging consists of tests that help to determine the extent of the disease. Fortunately, the majority of the testing is non-invasive and can be completed in a day. Staging most commonly includes: bloodwork and urinalysis (to assess the overall organ function and ensure that there are not any concerns for chemotherapy), needle aspiration of the enlarged lymph nodes, chest radiographs (x-rays), abdominal radiographs (x-rays) or abdominal ultrasound, immunophenotyping (B cell vs T cell) and possible bone marrow aspiration.

The goal of treating lymphoma is to obtain a good or better quality of life for the pet and hopefully give them more time to be with their families. A cure is not typically achieved but we attempt to attain a remission, which means that all evidence of lymphoma has disappeared from detection by your pet's clinician.

## Types of Lymphoma

Lymphoma can be divided into five different forms depending on the primary or predominant site of the tumor:

- 1. External/Peripheral Lymph Nodes:** The most common form is involvement of one or more of the external lymph nodes. In many cases, the only noticeable sign is an enlargement of the lymph nodes under the neck, behind the knees or in front of the shoulders. In general, most patients do not feel sick or experience only very mild signs such as lethargy and/or decreased appetite. Other dogs may have more severe signs such as weight loss, vomiting, diarrhea, excessive thirst/urination, weakness or difficulty breathing. The severity of the signs depends upon the extent of the cancer and whether the cancer has caused changes in organ function. Other organs such as the liver, spleen and bone marrow can be involved or become involved as the lymphoma progresses.
- 2. Gastrointestinal Tract:** A second form is involvement of the gastrointestinal (GI) tract. Dogs with this form of lymphoma often experience vomiting, diarrhea, weight loss and/or a decreased appetite.
- 3. Mediastinal:** The mediastinum is a term used for a special aggregation of lymphoid tissue in the chest, just in front of the heart. Dogs with this form of lymphoma are often seen because of difficulty breathing or excessive urination/thirst due to elevated calcium levels secondary to the cancer.

4. **Cutaneous/Epitheliotropic:** Lymphoma can also develop in the skin which is known as cutaneous or epitheliotropic lymphoma. Dogs with cutaneous lymphoma may have flaky, scaly, reddened skin and are often itchy. They may also have masses in the skin which can ulcerate and cause discomfort. The footpads and gingival (oral mucosa) are often involved as well. Other organs such as lymph nodes, liver, spleen and bone marrow are variably involved.
5. **Bone Marrow:** If the lymphoid cancer is confined to the bone marrow the term used is leukemia. The clinical signs in dogs are usually related to the decreased numbers of normal cells such as red blood cells that carry oxygen, white blood cells that fight infection and platelets that help with blood clotting. All of these normal cells are made in the bone marrow. Anemia, infections and bleeding are common problems in patients with leukemia.

## Stages of Lymphoma:

Dogs with enlarged peripheral lymph nodes can be assigned a stage using the information gathered above.

**Stage I** is a single affected lymph node (this is rare).

**Stage II** is when only a set of lymph nodes is involved (also rare).

**Stage III** is when lymph nodes in the back and front half of the body are involved.

**Stage IV** is when the liver and spleen are involved in addition to the lymph nodes.

**Stage V** is when there is bone marrow involvement (or any location outside of liver, spleen and lymph nodes)

Most patients present as either a stage III or IV. There is also a sub-stage that refers to whether or not a patient is sick from their disease. Sub-stage 'a' is a dog with minimal symptoms while stage 'b' is a dog with significant symptoms (vomiting, diarrhea, loss of appetite, lethargy).

Lymphocytes can be broken down into two basic types – B and T cells. Each type has a different role in the immune system and can become cancerous. Knowing the type may change the prognosis and treatment; therefore, additional testing known as immunophenotyping can be performed to determine which type of lymphoma a patient has. The different options for immunophenotyping include flow cytometry, PARR or immunohistochemistry.

The results of the staging and the immunophenotyping can help determine the prognosis and best treatment protocol for an individual dog.

## Treatment and Prognosis

Chemotherapy is the mainstay of treatment for lymphoma. If left untreated, most dogs succumb to the disease within 1-2 months. Fortunately, lymphoma is very sensitive to chemotherapy and up to 85% of dogs treated with a multi-drug protocol will go into a complete remission. The definition of a complete remission is the disappearance of detectable cancer with physical exam and diagnostic tests. A remission is NOT a cure; but, it does allow your pet to experience a good quality of life for a period of time. Because a cure is rarely achieved, chemotherapy continues beyond when clinical remission is noted. When a pet comes out of remission, you may choose further treatment to attain a second or third remission, but this largely depends on the pet's clinical status at the time of relapse and how they tolerated their previous chemotherapy regimen(s).

The length of remission depends upon many factors including: the primary tumor site, how sick an animal is at the time of diagnosis, whether or not this is a B or T cell form of lymphoma and the extent of disease (stage). For those dogs that have the most common type of lymphoma (external lymph node enlargement of the B cell type), the average first remission time is usually around 8-10 months with an overall survival time of approximately 12-18 months. About 15-20% of dogs will live longer than 2 years and less than 5% of dogs are cured.

Chemotherapy protocols are dependent on a number of factors and the best protocol for one pet may not be appropriate for another. Factors that will influence the overall outcome of treatment include: location of lymphoma (peripheral lymph node form has the best outcome), whether or not a patient is sick from their disease (healthy patients do better), whether or not there is bone marrow involvement (no bone marrow involvement has a better prognosis), whether or not there is a high blood calcium level (normal calcium levels are better), and the immunophenotype (B cell lymphomas tend to be better).

#### Treatment options:

- Multi-drug protocol, which includes four to five different chemotherapy drugs which are alternated in order to reduce the chance that the tumor cells will become resistant as well as to reduce the risk of potential side effects. This type of protocol is often referred to as a CHOP-L protocol or University of Madison-Wisconsin protocol. These drugs include Elspar (L-asparaginase), Vincristine (Oncovin), Cytoxan (Cyclophosphamide), Adriamycin (Doxorubicin), and Prednisone. Protocols that use several different drugs are generally considered to be superior to protocols that use only one or two drugs. Initially, treatments are given frequently (once weekly) but depending upon the response and protocol, treatments are then spread out to every other week or every third week and/or discontinued. With this protocol 80-90% of patients will go into a complete remission with an average survival time of 12-18 months.
- Single agent Adriamycin. This is one of the most effective single agent therapies where 50-70% of dogs will go into remission with an average survival time of 6-9 months. Due to the risk for dose cumulative heart toxicity an echocardiogram (ultrasound of the heart) may be indicated for some dogs. This protocol is administered once every 3 weeks for 5-6 doses.
- COP (Cytoxan, Oncovin (vincristine), prednisone) is a combination protocol that includes oral and injectable chemotherapy that is administered weekly for 4 weeks, then going to once every 2-3 weeks after as long as remission is achieved. Around 50-70% of dogs will respond to this therapy for an average of 6-9 months.
- MOPP (Mustargen, Oncovin (vincristine), Procarbazine, Prednisone) is a multi-agent protocol that consists of two injectable agents (mustargen and vincristine) and two oral chemotherapy agents (procarbazine and prednisone). The goal is to treat for a total of 6-8 doses and then monitor patients who achieve a complete remission.
- L'asparaginase and CCNU (Lomustine) combination or CCNU alone. CCNU can cause increases in liver values (specifically ALT). Due to this, patients are started on a liver supplement called Denamarin which has been shown to help keep the liver protected. During and after treatment, the patient's liver enzymes will be monitored. This protocol is administered once every 3 weeks for 6-8 doses.
- Prednisone alone can make dogs feel better and decrease the size of the lymph nodes but the duration of positive benefit is relatively short. With Prednisone alone, the average survival time is between one to three months.

If a patient comes out of remission, we can try to put them back into remission using either new combinations of the same drugs or different drugs altogether. For dogs that have finished the short-term multi-drug protocol, we may consider restarting a protocol using these same drugs. Unfortunately, the chances of obtaining a second remission are lower (60-70%) and the length of remission is often shorter (generally half as long as the first remission).

## Potential Side Effects

Most dogs will tolerate their chemotherapy well and have minimal side effects. Significant side effects are seen in roughly 10% of patients treated. These may include nausea, vomiting, loss of appetite, diarrhea, extreme tiredness, low white blood cell counts and/or infection. Side effects generally occur within the first week of treatment (3-5 days for GI and 7-10 for low white blood cell counts). These signs typically resolve within 24-48 hrs and sometimes without any treatment. Hair loss or slow hair growth may also occur in certain instances although this is not a big issue in our patients. Adriamycin can cause dose cumulative damage to the heart muscle if administered more than a certain number of times; however, by limiting the number of treatments and monitoring the heart, the risk of heart damage is very low. Cytoxan can cause irritation to the bladder wall in a small percentage of dogs. If this occurs, you will see changes in urination such as blood in the urine, straining to urinate and/or frequent urination.

## Take Home:

Please know that we are always keeping your pet's quality of life front and center. The hope is to provide you with as much additional good quality time as possible. The goal of therapy is to keep your pet happy and minimize discomfort. Although some animals may experience transient discomfort from therapy, cancer treatment for most pets is accomplished without major distress or detracting from your pet's enjoyment of life. When the cancer does start to progress to a point where your pet's quality of life is declining, your veterinary team is here to discuss when euthanasia is the best option and to help you through that difficult time.