

## Mast Cell Tumors in Dogs

These notes are provided to help you understand the diagnosis or possible diagnosis of cancer in your pet. For general information on cancer in pets ask for our handout "What is Cancer". Your veterinarian may suggest certain tests to help confirm or eliminate diagnosis, and to help assess treatment options and likely outcomes. Because individual situations and responses vary, and because cancers often behave unpredictably, science can only give us a guide. However, information and understanding for tumors in animals is improving all the time.

We understand that this can be a very worrying time. We apologize for the need to use some technical language. If you have any questions please do not hesitate to ask us.

### ***Mast cell biology***

Mast cells originate in the bone marrow but complete their development in peripheral tissues. They are found in all tissues of the body but are concentrated in the skin, respiratory tract and digestive tract. Mast cells interact with cells of the immune (protective) system producing allergic type antibodies (IgE), presenting foreign molecules (antigens) to immune stem cells and recruiting certain cells (phagocytes) to engulf foreign or invading material. As well as being a cellular barrier to external agents, mast cells have a regulatory function on cutaneous nerves, blood circulation, fibrous tissue and other immune cells. They are therefore important in allergic responses, tissue remodelling, wound healing and non-allergic skin diseases. Mast cells in hair follicles also help to regulate the cyclical activity of those follicles.

Not surprisingly, with all these functions, mast cells are not a single cell type. In dog skin, most are a highly reactive type called "CT-mast cells".

### ***What is a mast cell tumor?***

This is a tumor originating from the dogs mast cells. These tumors include both benign (relatively harmless) and highly malignant (more dangerous and spreading) types. Some are multiple. Recurrence of the tumor and spread to other parts of the body (metastasis) is possible with some types.

Not surprisingly, with all these functions, mast cells are not a single cell type. In dog skin, most are a highly reactive type called "CT-mast cells".



Image courtesy of Jan Hall, BVM&S, MS, MRCVS, DipACVD, Clinical Dermatology, Ontario Veterinary Clinic

### ***What do we know about the cause of mast cell tumors?***

The reason why a particular pet may develop this, or any cancer, is not straightforward. Cancer is often seemingly the culmination of a series of circumstances that come together for the unfortunate individual.

For humans, research has indicated that abnormalities of certain receptors (key-lock mechanisms) on the surface of mast cells may contribute to some of these tumors. Other causes are overproduction of body factors that stimulate mast cell proliferation (such as Stem Cell factor, SCF); and cellular genetic mutations and gene malfunctions. Details of these are beyond the scope of these notes.

### ***Is this a common tumor?***

Mast cell tumors are “common” (about 90 dogs for every 100,000 dogs in any year). This is still a very small number in the overall population but is very high compared with other neoplasia.

Some breeds are more susceptible. Mast cell tumors are particularly common in Boxers, Bull Terriers and Labrador Retrievers. They are rare in German Shepherd dogs.

The median age is 8-9 years but cases can occur at any age including in puppies.

Occasionally they involve the internal organs. They can be multiple.

### ***How will this cancer affect my pet?***

The most obvious effect of most mast cell tumors is a lump. The tumor cells produce many chemical mediators (histamine, proteoglycans, neutral proteases and chemotactic growth factors). These mediators have local effects on blood vessels and cells of the immune system that may make the tumor look like an inflammatory reaction or infection. Tumors often bleed and may vary in size from day to day. The chemical mediators may induce inflammatory effects elsewhere in the body, such as in the stomach causing gastritis.

Weight loss due to loss of body fat and muscle is commonly associated with malignant (spreading) tumors and the immune system is often damaged.

### ***How is this cancer diagnosed?***

These tumors are called the great imitators, as they can clinically resemble many other tumor types.

Pre-surgical cytology (microscopic examination of cell samples) is a useful technique to identify this tumor and plan surgery. Some grades of the tumor are very diffuse and not well demarcated from normal surrounding tissue, so that unusually wide surgical margins around the obvious lump are required for complete excision of the tumor.

Cytology (examination of cell samples drawn from the lump through a needle) cannot be used for grading to predict biological behaviour or to indicate margins of mast cell cancer. Such information relies upon microscopic examination of the whole tumor (histopathology) which is done at a specialized laboratory by a veterinary pathologist.



### ***Types of mast cell tumor and probable outcome***

Confusingly, mast cell tumors (mastocytomas) are not divided as most tumors are into benign (non-spreading) and malignant (life-threatening, spreading) tumors but are graded

into three groups. Grading is subjective but both it and staging (the extent of spread of the tumor) are predictive of tumor behavior. The information from the whole lump will also indicate whether the cancer has been fully removed.

#### *Well differentiated (grade I) tumors*

The cancerous mast cells are 'mature' (well differentiated) but these are paradoxically the least well defined tumors in terms of their borders and their diffuse nature makes excision difficult. They are usually clinical stage I: one tumor confined to the skin without spread to local lymph nodes ("glands"). Almost all this grade of tumor are benign.

#### *Intermediate, moderately-well differentiated (grade II) tumors*

Although clinical behavior of mastocytomas is related to histological grade, this grade is less easy to predict. Sixty-five percent are cured surgically but both recurrence and metastasis (tumor spread) are possible. Factors that make the outcome (prognosis) potentially less favorable include: clinical progression beyond stage I (spreading to multiple locations); a rapid growth rate; systemic illness; breed other than Boxer; and history of recurrence. Factors for a less favourable outcome also include tumor location (bone marrow, body organs, or at junctions of mucous membranes and skin); and some microscopic features.

#### *Poorly differentiated (grade III) tumors*

With this type of mast cell cancer both recurrence and metastasis are probable. Factors further reducing the probability of a favourable outcome are similar to those for the intermediate grade as above. Tumors of this grade are almost invariably fatal and at least five times more aggressive than the intermediate grade.

### ***Is there anything else that may help to predict what will happen to my dog?***

#### *Tumor Grading (see above)*

Histopathological grading is currently used to help forecast the outcome of an individual case. It is however somewhat subjective so researchers are looking for molecular markers that will better differentiate normal and malignant mast cells and provide improved prognostic information.

#### *Tumor Staging*

Current staging methods (lymph node palpation and needle aspiration biopsy, abdominal ultrasound and bone marrow cytology) are of limited use for prognosis as "normal" mast cell populations in sites such as liver, spleen and bone marrow cannot be differentiated from metastatic disease. Research to find molecular markers to detect malignant mast cells is a key element to resolving this dilemma. Pending standardized staging protocols, staging to assess tumor spread may include lymph node needle biopsy, abdominal ultrasound and bone marrow biopsy.

### ***What types of treatments are available?***

Surgery to remove the tumor with a wide margin of tissue around the lump is the first treatment whenever possible for all grades of mast cell tumors.

#### *Well differentiated (grade I) tumors*

Almost all this grade are benign and can be cured surgically if margins of apparently normal tissue surrounding the obvious tumor can be safely removed. In one survey, 83% dogs were alive four years after surgery and only 10% of the deaths in that period were tumor related.

#### *Intermediate, moderately well differentiated (grade II) tumors*

With surgical treatment alone, 44% of dogs survived over four years in one survey. Additional therapy may be considered for incompletely excised tumors, high-grade tumors, and those with features warranting a poor prognosis such as rapid reappearance.



Chemotherapy (drug treatment) is usually reserved for use if the primary tumor is life-threatening or when there is disseminated disease. The optimum chemotherapy protocol for treatment is unknown but there are drugs that can be used. If it is considered necessary to try this approach, your veterinarian will discuss the pros and cons with you.

Irradiation, usually available only at specialized centers, can be more effective than chemotherapy but, after irradiation, 12% of dogs with tumors of this grade will still be expected to develop metastatic disease within a year. Radiation is used primarily to treat incompletely resected tumors. Radiation therapy may be warranted to improve quality of life even where a 'cure' is unlikely, but this requires consideration of many factors.

Photodynamic therapy (PDT) is a localized treatment (of limited availability) that relies on the interaction of a photosensitizing agent and light. Results to date have been similar to those achieved with radiation.

#### *Poorly differentiated (grade III) tumors*

The outcome, even with surgery, is very poor with this grade of tumor. Less than 10% dogs are likely to survive more than one year and many will succumb within a much shorter time (average 14 weeks).

Responses to chemotherapeutic drugs alone or in combinations have generally been poor at this stage, and side effects have to be considered.

Irradiation, where available, is more effective than chemotherapy but, even after irradiation, about 55% of dogs with poorly differentiated tumors will develop metastatic disease within a year. Local recurrence is even more frequent.

Gastrointestinal signs due to release of chemical substances by the mast cells can be treated symptomatically with H<sub>2</sub> receptor antagonists such as cimetidine or calcium channel blockers such as omeprazole.

#### ***Can this cancer disappear without treatment?***

Mast cell tumors rarely disappear without treatment but some well differentiated tumors of this type occur in multiple sites in young dogs and may sometimes regress spontaneously. This condition is sometimes called 'mastocytosis'. These 'tumors' may be not true cancers but a hyperplasia (non-cancerous overgrowth). Occasionally (even at a few weeks of age), there may be hundreds of similar lesions. Additionally, Boxers have large numbers of mast cells in some inflammatory reactions (particularly on the ears). These are not neoplastic but

they cause severe rash (urticaria) and pruritus (itching), and are poorly responsive to treatment.

Poorly differentiated mast cell tumors do not disappear spontaneously.

### ***How can I nurse my pet?***

This tumor is often pruritic. Preventing your pet from rubbing, scratching, licking or biting the tumor will reduce itching, inflammation, ulceration, infection and bleeding. Any ulcerated area needs to be kept clean.

After surgery, the operation site similarly needs to be kept clean and your pet should not be allowed to interfere with the site. Any loss of sutures or significant swelling or bleeding should be reported to your veterinarian. Hematoma (bleeding) in the surgical wound is not uncommon after surgery for this tumor. If you require additional advice on post-surgical care, please ask.



### ***When will I know if the cancer is permanently 'cured'?***

"Cure" has to be a guarded term in any cancer.

Histopathology and the report of the veterinary pathologist will give your veterinarian the diagnosis that helps to indicate how an individual tumor is likely to behave (the prognosis) including the probability of local recurrence or metastasis (distant spread). Clinical staging tests may establish that such distant spread has occurred.

The absence of any recurrence beyond 6 months is encouraging, because recurrence usually occurs within a few months of surgery.

### ***Are there any risks to my family or other pets?***

No, this is not an infectious tumor and it is not transmitted from pet to pet or from pet to people.