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Staging Melanoma of the Oral Cavity or Skin in Dogs

Melanomas are typically pigmented tumors of the skin and mucous membranes. Some melanoma tumors may be nonpigmented (amelanotic).

A New Column

Diagnosing diseases and conditions may require a various array of diagnostic tests and modalities. This column discusses when a test or procedure is indicated as well as its advantages, disadvantages, economic impact, and reliability of results.

Early studies found that the World Health Organization (WHO) staging system for melanoma (see **Box**) provided prognostic information,¹ but more recent information suggests that these criteria should be combined with information from histopathology (especially the mitotic index).

Current recommendations for staging melanoma include:

- Detailed information on the location of the primary tumor
- Accurate tumor measurements and lymph node evaluation by cytology or biopsy
- Careful evaluation for metastasis by thoracic radiography, CT, or MRI
- Evaluation of the histopathology criteria listed above.

While such information will not provide an accurate prognosis for every canine patient with melanoma, it will allow the owner and oncologist to make a more individual treatment decision.

Physical Examination Indications

The physical examination is critical in staging

WHO Staging for Oral Melanoma*

Clinical Stage	Tumor	Node	Metastasis
I	< 2 cm	–	–
II	2–4 cm	–	–
III	> 4 cm or bone involvement	Yes	–
IV	Any	Any	Yes

*Also applicable to other sites, such as skin, digits, and lip

the tumor and establishing some prognostic criteria. One of the most important prognostic factors gained from the physical examination is **tumor location**.

A recent study distinguished between the behavior of melanomas of the feet and lips and the behavior of those of the skin and oral cavity, respectively. Tumors in haired-skin areas are generally benign (although there are exceptions), while tumors at mucocutaneous junctions, nail bed, and mouth are most often malignant, with the vast majority of oral melanomas being malignant. Median survival and mortality due to melanoma were 22 months and 30%, respectively, among dogs with

melanoma of the feet or lips, 5 months and 68% among dogs with oral melanoma, and 24 months and 7% among dogs with cutaneous lesions. When the tumor recurred or metastasized, it did so more rapidly for dogs with oral lesions (median, 2.5 months) than for those with toe/lip melanoma (5.3 months) or cutaneous melanoma (8.9 months).²

Another important prognostic factor gained from the physical examination is **the size of the primary tumor**. The size of an oral melanoma was associated with survival in a study that used radiation therapy as the primary treatment (**Table 1**, page 28).³

CT = computed tomography; MRI = magnetic resonance imaging; WHO = World Health Organization

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Table 1. Size of Oral Melanoma & Survival

Tumor	Median progression-free survival (mo)	1-year tumor-free survival (%)	3-year tumor-free survival (%)
Overall	8	36	20
T1 (< 2 cm diameter)	19	71	54
T2 (2–4 cm diameter)	6	28	12
T3 (> 4 cm diameter)	7	23	9



Most cutaneous melanomas are biologically benign, but biopsy and complete staging is necessary to make that determination. This 16-year-old dog had a benign melanoma and vestibular disease.



Cutaneous melanoma of the digits is more likely to be malignant than melanoma from other cutaneous sites, but in 1 study, 70% of patients did *not* die of melanoma. Therefore, biopsy and complete staging are needed to make an accurate prognosis.

Advantages

Easy to perform and minimally invasive; provides critical information for staging and prognosis

Disadvantages

None

Economic Impact

Minimal; it needs to be done for all patients.

Reliability of Results

Physical examination findings will often need to be illuminated by further staging (eg, imaging, biopsy) but are reliable if done carefully.

Minimum Database Indications

A complete blood count, baseline serum biochemistry panel, and urinalysis (with culture, if indicated) are always recommended for baseline staging of cancer, particularly if surgery,

chemotherapy, or multiple anesthetics (such as for radiation therapy) are anticipated.

Advantages

Easy to perform and minimally invasive; provides critical information for planning treatment and anesthesia

Disadvantages

None

Economic Impact

Minimal; it needs to be done for all older patients.

Reliability of Results

Results are reliable if testing is performed on serviced equipment and by qualified personnel.

Lymph Node Assessment Indications

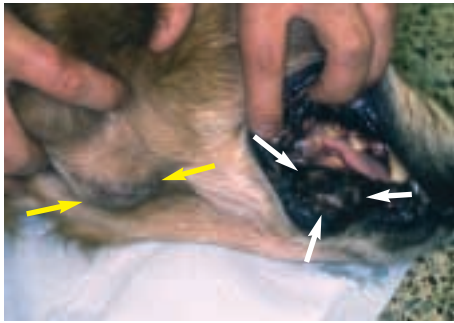
The metastatic rate is very high for oral melanoma, but the time to metastasis varies. At diagnosis, the mandibular lymph nodes (ipsilateral and contralateral) should be palpated and fine-needle aspiration performed for cytologic examination. Since the oral cavity drains to the parotid and retropharyngeal lymph nodes, these nodes can be assessed by CT (and possibly ultrasonography) if advanced imaging is planned.

Evidence of atypical melanocytes or melano- phages on cytology suggests metastasis. Suspicious results on aspiration cytology should be confirmed by surgical biopsy. Note that although 60% of enlarged lymph nodes had cytologic evidence of metastasis in a study of 100 dogs with oral melanoma, metastases were detected in 40% of normal-size lymph nodes.⁴ Thus, even normal-size lymph nodes should be aspirated or biopsied. The mandibular nodes are the most commonly affected site for oral melanoma; however, when melanomas of other sites are diagnosed, the regional lymph nodes should be similarly assessed.

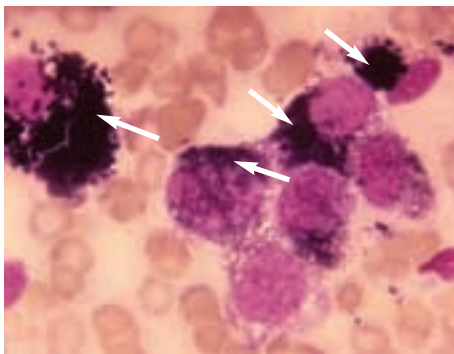
Advantages

Easy to perform and minimally invasive; provides critical information for staging and prognosis

CT = computed tomography; MRI = magnetic resonance imaging



Oral melanomas have a high metastatic rate, as seen in this 14-year-old golden retriever. To accurately assess the primary lesion (*white arrows*), physical examination may need to be complemented with radiography and, possibly, CT if aggressive resection is planned. Note the enlarged mandibular lymph node (*yellow arrows*) that should be aspirated for cytology or biopsied along with the primary lesion.



Cytology from a primary melanoma may allow pre-operative diagnosis, as in this preparation showing prominent melanin granules in the tumor cells (*arrows*). Biopsy is still necessary for histologic grading that is used in conjunction with staging to provide an accurate prognosis for the patient.

Disadvantages

Cytology results may be equivocal and biopsy may be required to definitively determine whether metastasis is present.

Economic Impact

Cost of cytology and procedure

Reliability of Results

Cytology is reliable if fine-needle aspiration is performed carefully, but “negative” results could be misleading.

Biopsy

Indications

Although histopathology is required for definitive diagnosis of melanoma, the index of suspicion should be high in an old dog with a friable oral mass or a dog with a cutaneous (especially digital) pigmented lesion. For most melanomas, the diagnosis may be made by finding melanin granules in the cytoplasm on light microscopy. Some immunohistochemical markers (S-100, Melan-A, HMB-45) have been explored for their value in diagnosing melanoma when the tumor is poorly pigmented and poorly differentiated.

A recent study found shorter survival for dogs with melanomas from any site that was larger, had high numbers of mitotic figures per 10 high-powered fields, had marked nuclear atypia, and had more inflammation or necrosis (these characteristics were used to calculate a numeric score; see **Table 2**).²

Biopsy of the regional lymph nodes, even those not enlarged, at the time of lesion biopsy is recommended because it will affect staging and may direct therapy. One study found that dissection of the lymph nodes at surgery increased the number of dogs diagnosed with metastatic disease.⁵

Advantages

Can be performed safely and provides critical information for staging and prognosis

Disadvantages

Requires general anesthesia and careful planning so as not to negatively affect future definitive surgery attempts; best to consult with the surgeon or radiation oncologist who will be performing definitive treatment

Economic Impact

Costs of anesthesia, procedure, and pathology, as well as potential additional costs of immunohistochemistry if needed

Reliability of Results

Extremely reliable when sample is properly collected and fixed

Table 2. Melanoma Histopathology Score as a Predictor of Survival

Variable	Score
Mitotic index (<i>n</i> per 10 hpf)	Numeric
Nuclear atypia (<i>n</i> , 1–10)	Numeric
Deep intralesional inflammation:	
Yes	0
No	1
Intralesional necrosis	
Yes	0
No	1
Tumor size (cm)	
< 0.5	0
0.5–1	1
> 1	2

SCORE: < 10 = benign, ≥ 10 = malignant
Higher risk of recurrence and/or metastasis with scores higher than 9

Not important: Nuclear diameter, intraepithelial melanocyte proliferation, junctional activity, giant cells, cell type
hpf = high-powered field

Imaging of Tumor & Distant Sites

Indications

Fine-detail radiographs of the affected area, including the digit or the dental arcade (depending on site of primary tumor), provide information on the size and invasiveness of the melanoma. Radiographs of the affected digit show lysis of P3 in approximately 80% of dogs with subungual squamous cell carcinoma. This is in contrast to digital melanomas, which rarely cause bony destruction (5% of cases). CT or MRI will more accurately delineate bone involvement and should be considered if the tumor margins are uncertain on physical examination or radiography.

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Thoracic radiographs may indicate pulmonary metastasis at the time of diagnosis and should be obtained before definitive treatment. Pulmonary metastasis, however, frequently occurs late in the disease.^{6,7} Thoracic CT is more sensitive at detecting pulmonary metastases and should be considered when access is possible and finances permit.

Melanoma may also spread systemically to other sites, and metastasis has been reported in the kidney, myocardium, and brain.⁸ If involvement of other sites is suspected (based on results from baseline blood analysis or physical examination and history), then imaging (abdominal ultrasonography, CT, or MRI) of the abdomen or central nervous system is warranted.

Advantages

Can be performed safely and provides critical information for staging and prognosis

Disadvantages

May require sedation for radiography and ultrasonography; will require general anesthesia for CT or MRI, as well as access to facilities. Radiography and CT carry a risk for radiation exposure. It is worth consulting with the surgeon or radiation oncologist who will be performing the definitive treatment to ensure correct views are obtained.

Economic Impact

Costs of anesthesia and procedure can be considerable, but these tests will allow for more accurate treatment decisions, minimizing risks for toxicity or inadequate treatment of tumor.

Reliability of Results

Extremely reliable if performed on serviced equipment and by qualified personnel. ■

See **Aids & Resources, back page, for references, contacts, and appendices.**
Article archived on www.cliniciansbrief.com

CT = computed tomography; MRI = magnetic resonance imaging



Dechra to Distribute Oxyglobin

Dechra Veterinary Products (www.dechra-us.com) has secured exclusive U.S. marketing and distribution rights for Oxyglobin Solution (hemoglobin glutamer-200 [bovine]) from Biopure Corp (www.biopure.com). Oxyglobin is approved by the FDA for veterinary use for the treatment of canine anemia. Dechra will market Oxyglobin in 60-mL and 125-mL single-dose infusion bags.—*Press release 5/14/08*

Big News for Little Pets

The American Veterinary Medical Association has provided conditional recognition for a new veterinary specialty—Exotic Companion Mammal (ECM)—focusing on small mammals including rabbits, ferrets, guinea pigs, mice, and other small mammals, commonly known as “pocket pets.” The ECM practice area also includes more unusual small pets, including hedgehogs and sugar gliders. Applicants will be required to have 6 years experience in the field, letters of reference, relevant education, publications in the field, and pass a 2-day examination. The ECM specialty has between 4 and 10 years to petition for full recognition from the AVMA. For more information, visit www.avma.org. —*Press release 4/24/08*

Industrial Chemicals Contaminate Cats & Dogs

Analysis of blood and urine from 20 dogs and 37 cats in a study by the Environmental Working Group (www.ewg.org) found that the chemical body burden of companion animals is substantially higher than is typical for humans, with 2.4 times the levels of stain- and grease-proof coatings (perfluorochemicals) in dogs, 23 times more fire retardants (PBDEs) in cats, and more than 5 times the amount of mercury usually found in humans. Dogs and cats were contaminated with 48 of 70 industrial chemicals tested. Health risks in pets have not been studied but the chemicals are linked to serious health effects in laboratory data on human populations.—*Press release 4/17/08*

Environmental Study

Approval Granted

Cancer Imaging & Research Center Planned

Texas A&M University College of Veterinary Medicine has received approval to build a veterinary imaging and cancer research center. Plans for the \$4.5 million project include an 8000-square-foot building for small-animal and equine patients and a linear accelerator.—*Press release 5/2/08*