



SET THE STAGE

After it has been confirmed that a patient has cancer, several staging tests can help determine the likely spread and behavior (grade) of a tumor, as well as the type of cancer.

CONTINUING EDUCATION

ONCOLOGY

Staging Cancer: Digging Deeper Than the Diagnosis

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Staging is a crucial part of the diagnostic process for cancer or probable cancer and should be performed before any treatment is initiated. While staging is often considered extraneous or unnecessary, the tests used give the veterinary team the best overall picture of the cancer the patient is facing and can aid in diagnosis, prognosis, and treatment recommendations. Many of these tests can be performed before referral to a veterinary oncologist.

Diagnosing and staging cancer are a multistep process, and no single test is the most important in all cases. Establishing if a patient has cancer is the first step, and several staging tests can help determine the likely spread and behavior (grade) of a tumor, as well as the type of cancer.

CANCER TERMINOLOGY

A cancer *diagnosis* identifies the specific type of tumor: round cell, sarcoma, or carcinoma. *Staging* is the determination of the extent of both local disease and tumor spread throughout the body (*metastasis*). The most common staging tests are the physical examination, laboratory tests, tissue sampling (cytology or histology), and diagnostic imaging.

Grading a tumor is evaluating the cells and describing how abnormal they look under a microscope. The tumor grade is an indicator of how aggressive the tumor will be; that is, how rapidly it is expected to grow and how likely it is to metastasize. It is important to differentiate tumor stage versus tumor grade.

IMPORTANCE OF STAGING

Obtaining tissue samples and information before treatment allows for the best possible outcome. Knowing if a tumor has metastasized beyond the primary location can enable planning for more extensive surgery or for multimodal treatment with surgery, chemotherapy, and/or radiation therapy. By understanding tumor behavior and the route by which a specific tumor type may spread, oncologists can recommend the most valuable staging test for that cancer.

One of the most common mistakes in veterinary cancer medicine is starting a patient with lymphoma or another round cell tumor on corticosteroids after diagnosis but before staging.¹ While this can make the patient feel better and reduce the cancer burden, it can also make determining the initial stage impossible and can lead to an inaccurate prognosis.

Full cancer staging can also help identify any concurrent diseases, particularly in geriatric patients. For example, thoracic radiographs are



clinically indicated to screen for lung metastasis in patients with appendicular osteosarcoma. While this tumor rarely spreads to the abdomen, performing abdominal ultrasonography in these patients may reveal abnormalities caused by another disease process that could affect the treatment plan. **TABLE 1** lists staging tests for some common types of cancer.

STAGING SYSTEMS

Many cancers are staged using the same system, but there are exceptions. The most common cancer in veterinary patients, lymphoma, has its own specific staging system. All staging evaluates the site, size, cell type, and grade of the primary tumor; lymph node involvement; and whether metastasis is present. While not all cancers use a staging system, understanding the common systems can help when assisting the veterinarian or educating the client.

TNM

The TNM system refers to the primary tumor (T), lymph nodes (N), and metastasis (M).³ Tumor size and extent are classified into 4 categories (T1–T4) based on tumor type. Regional lymph node involvement (N1–N3) describes size and presence of palpable lymph nodes. The addition of subgroup a or b designates whether the lymph node is metastatic or not. Distant metastasis is simply noted as absent (M0) or present (M1). Specific descriptions for each category in the system differ by tumor type. **BOX 1** contains the TNM descriptions for canine and feline skin tumors.

Lymphoma

Owing to the nature of lymphoma and its presence in the immune system, it is considered a systemic disease regardless of primary location, and its presence in multiple locations and organs is not considered metastatic. The 5 stages of lymphoma are based on the organs involved, and its 2 substages, a and b, depend on clinical signs (**BOX 2**).³ Prognosis is the same for patients with stage I through IV disease and does not often change therapy choice. Patients with the most advanced disease, stage V, and those with substage b have a poorer prognosis owing to a decreased response to treatment.

PHYSICAL EXAMINATION

It may seem obvious, but the physical examination is an important part of staging. All abnormalities should be noted. Any masses or lesions should be described and measured. If there are multiple masses, a body map should be started to track them all. All lymph nodes should be palpated and their size noted. If any are enlarged, they should be measured. Any physical examination abnormalities should be investigated to see if they are attributable to the cancer diagnosis. A rectal examination is part of a full physical examination in all animals, and doubly so in cancer patients.

LABORATORY TESTS

Lab work, such as a serum biochemistry panel, complete blood count (CBC), and urinalysis, is part of routine veterinary care. In veterinary oncology, these

TABLE 1 Recommended Staging Tests for Common Cancer Types²

CANCER TYPE	STAGING TESTS
Lymphoma	<ul style="list-style-type: none"> • Serum biochemistry panel, complete blood count, and urinalysis • 3-view thoracic radiographs • Abdominal ultrasonography • Immunophenotyping
Mast cell tumor	<ul style="list-style-type: none"> • Serum biochemistry panel, complete blood count, and urinalysis • 3-view thoracic radiographs (depending on tumor location) • Abdominal ultrasonography • Local lymph node cytology • Splenic cytology
Melanoma	<ul style="list-style-type: none"> • Serum biochemistry panel, complete blood count, and urinalysis • 3-view thoracic radiographs • Local lymph node cytology
Osteosarcoma	<ul style="list-style-type: none"> • Serum biochemistry panel, complete blood count, and urinalysis • 3-view thoracic radiographs
Hemangiosarcoma	<ul style="list-style-type: none"> • Serum biochemistry panel, complete blood count, and urinalysis • 3-view thoracic radiographs (depending on tumor location) • Abdominal ultrasonography

BOX 1**TNM System for Canine and Feline Skin Tumors³****Primary Tumor (T)**

- T0** No evidence of tumor
- Tis** Carcinoma in situ
- T1** Tumor <3 cm in diameter; superficial
- T2** Tumor 3–5 cm in diameter or with minimal invasion despite size
- T3** Tumor >5 cm in diameter or with invasion of subcutis despite size
- T4** Tumor invading beyond subcutis (fascia, muscle, bone, cartilage)

Regional Lymph Nodes (N)

- N0** No evidence of lymph node involvement
- N1** Movable enlarged lymph nodes on same side of body
- N2** Movable enlarged lymph nodes on opposite side of body or bilateral
- N3** Fixed lymph nodes
- a** Nonmetastatic lymph node
- b** Metastatic lymph node

Distant Metastasis (M)

- M0** No evidence of distant metastasis
- M1** Detectable distant metastasis

Complete Blood Count

In cancer staging, the most important components of the CBC are the red blood cell (RBC) and platelet counts. Anemia can be the first indication that the cancer has infiltrated bone marrow and is destroying tissue. Anemia and thrombocytopenia are most commonly associated with hematopoietic cancers (lymphoma and leukemia) but can also be seen with mast cell tumors (MCTs) and hemangiosarcomas.⁶ An increase in the RBC count (polycythemia) can be present with renal tumors as a PNS.

Because the white blood cell (WBC) count can be affected by many factors, it is less important as a staging tool. Chemotherapy can significantly decrease the WBC count, while many cancers, diseases, or even stress, can cause elevations in neutrophils. Significant increases in WBCs are seen in patients with leukemia; in these cases, the differential is valuable to identify which WBC count is elevated.

In general, however, the CBC does not affect prognosis, and the counts themselves are not the important factor in staging, but rather are indicators that additional tests are needed.

Urinalysis

Urinalysis is useful for fully evaluating renal function. In patients with urinary bladder tumors, the presence

tests are rarely used to diagnose cancer. They are used instead to complete the medical snapshot of the patient at the time of diagnosis. Additional tests can be added based on tumor type or abnormalities noted.

Serum Biochemistry Panel

Abnormalities in biochemistry values are multifactorial in cancer staging. The effects of concurrent diseases should be factored in or the presence of such diseases ruled out. When evaluating elevations in hepatic or renal values, it is important to know if the diagnosed cancer type metastasizes to the liver or kidneys. Certain cancers can cause paraneoplastic syndromes (PNSs). These are clinical signs that accompany cancer but do not correlate to the location of the primary tumor or metastasis. The most common PNS is hypercalcemia, which is often associated with lymphoma or apocrine gland anal sac adenocarcinomas.^{4,5} While this finding does not alter the stage, it can be a negative prognostic indicator.

BOX 2**Lymphoma Staging System³**

- Stage I** Involvement of a single lymph node
- Stage II** Involvement of multiple lymph nodes in the same region
- Stage III** Generalized peripheral lymphadenopathy
- Stage IV** Involvement of liver and/or spleen
- Stage V** Involvement of bone marrow and/or other organ systems (i.e., central nervous system, eyes)
- Substage a** Without systemic signs
- Substage b** With systemic signs

of bacteria can signify a concurrent urinary tract infection. In these cases, the tumor acts as a point of origin and place where bacteria can multiply. However, neoplastic cells are not often found in urine; therefore, urinalysis does not generally provide information on tumor stage or grade. Even in cases of urinary bladder tumors, the presence of inflammatory transitional cells is not conclusive for cancer.

Additional Tests

In specific cases, additional laboratory tests may be warranted. They may be prompted by abnormalities on a general screening test, such as proteinuria. If liver values are elevated, coagulation testing is recommended prior to aspirating cytology samples from the liver. In cases of thyroid or parathyroid tumors, additional thyroid testing can determine if the tumor is functional.

CYTOLOGY

Fine needle aspiration (FNA) and biopsy (incisional or excisional) are performed routinely to diagnose cancer, as well as for staging purposes (**FIGURE 1**). Cytology is used more frequently than histopathology for staging owing to ease of sampling and less need for anesthesia or sedation. Knowing common routes of metastasis can direct the veterinary team where to sample for neoplastic cells. Visual or palpable abnormalities may not be present with early spread; therefore, FNA of likely organs is useful as a normal part of staging for specific tumor types. Many tumors—such as oral melanoma—spread to the local lymph node(s)



FIGURE 1. Fine needle aspiration of a mass over the left hock of a dog. A mast cell tumor was diagnosed based on cytology.

(**FIGURE 2**) or—as with MCTs—to the spleen, since the spleen is part of the lymphatic system.

Bone marrow aspiration can confirm neoplastic infiltration suggested by CBC abnormalities. Bone tumors can also be aspirated to differentiate between primary and metastatic lesions. The location of the bone tumor is important, as primary appendicular osteosarcomas generally develop in specific locations. A good rule of thumb is to remember that primary tumors are found “away from the elbow and toward the knee.”⁷ Cytology of metastatic lesions can aid in locating the primary tumor.

IMMUNOPHENOTYPING

Immunophenotyping is used to determine the cell origin of hematopoietic tumors. It is most often used to

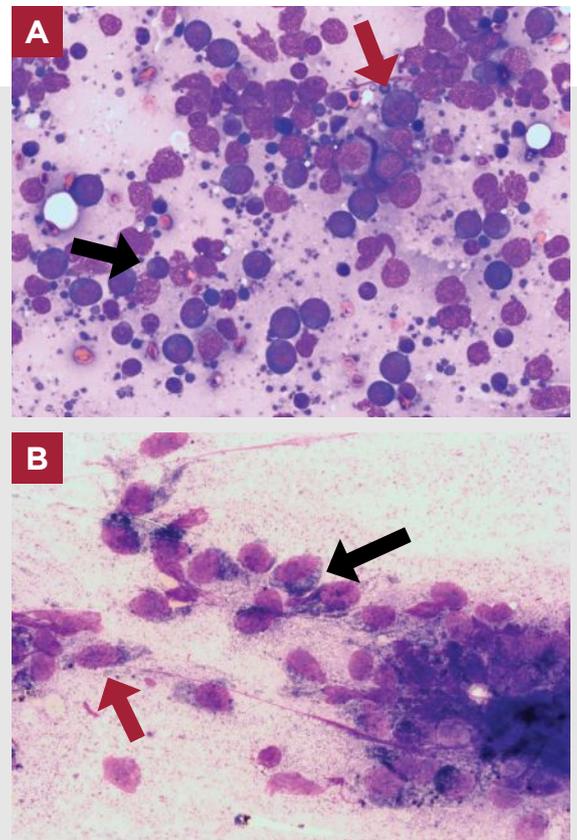


FIGURE 2. (A) Cytology of the right mandibular lymph node of a dog consistent with lymphoma. There are a few red blood cells, as well as small (**black arrow**) and large (**red arrow**) lymphocytes. **(B)** Cytology of the left mandibular lymph node of a dog consistent with malignant melanoma. There are a few red blood cells, macrophages, and neutrophils, but irregular spindle-shaped cells (**red arrow**) predominate. The cytoplasm contains greenish-black melanin granules (**black arrow**).

differentiate between B-cell and T-cell lymphoma as part of staging because T-cell lymphoma carries a poorer prognosis and can be more resistant to treatment.¹ It can also aid in distinguishing between stage V lymphoma and acute leukemias.

Immunophenotyping can be performed on aspiration samples, as well as on existing cytologic and biopsy samples using special stains.

HISTOPATHOLOGY

Biopsies are performed regularly in diagnosing cancer. It is preferable to obtain an aspirate and diagnosis from cytology prior to surgical removal because guidelines exist for removing different types of tumors to ensure the best chance of complete removal and possible cure.^{8,9}

Excisional Biopsy

When it comes to staging, local lymph node removal is the only type of excisional biopsy used. This practice is

standard in human medicine, and a pathologist is often available during surgery, even in the operating room, to verify metastasis. In veterinary medicine, lymph nodes are usually only removed when they are in the surgical field and appear grossly metastatic, such as during removal of a limb for osteosarcoma or during mastectomy or removal of an abdominal mass. When possible, surgical removal of the tumor should be performed after diagnosis and other staging procedures, not as a form of excisional biopsy.

Incisional Biopsy

Incisional biopsies are useful tools in staging tumors that do not exfoliate well enough to provide a definitive diagnosis or in grading tumors to aid in surgical planning and postsurgical treatment. For example, MCTs should be graded with histopathology prior to full surgical excision if possible. Low-grade MCTs can be cured with complete excision, while grade III tumors need follow-up radiation and possibly chemotherapy even with complete removal.¹⁰

DIAGNOSTIC IMAGING

Imaging is the most common and well-known test for cancer spread. Thoracic radiographs are commonly referenced as simply performing a “met check” in most hospitals. Ultrasonography, computed tomography (CT), and magnetic resonance imaging (MRI) all have their specific uses and can be preferable depending on cancer type.

Radiography

Radiographs are the most widely available and used staging tools. Many tumor types metastasize to the lungs; however, thoracic radiographs should be taken to evaluate for any concurrent diseases or age-related changes even in patients with cancer types that are not known to metastasize to the lungs. Metastatic disease can appear as solitary or multiple nodules or as a diffuse pattern (**FIGURE 3**). Sternal and thoracic lymphadenopathy can also be seen on radiographs. Submission of radiographs to a radiologist for review is preferred to ensure nothing is missed.

Radiographs can also aid in obtaining a diagnosis, and digital radiography has increased their diagnostic quality. In a hypothetical example, a dog presents with an undiagnosed oral mass along the gumline. Three-view thoracic radiographs are obtained, and small

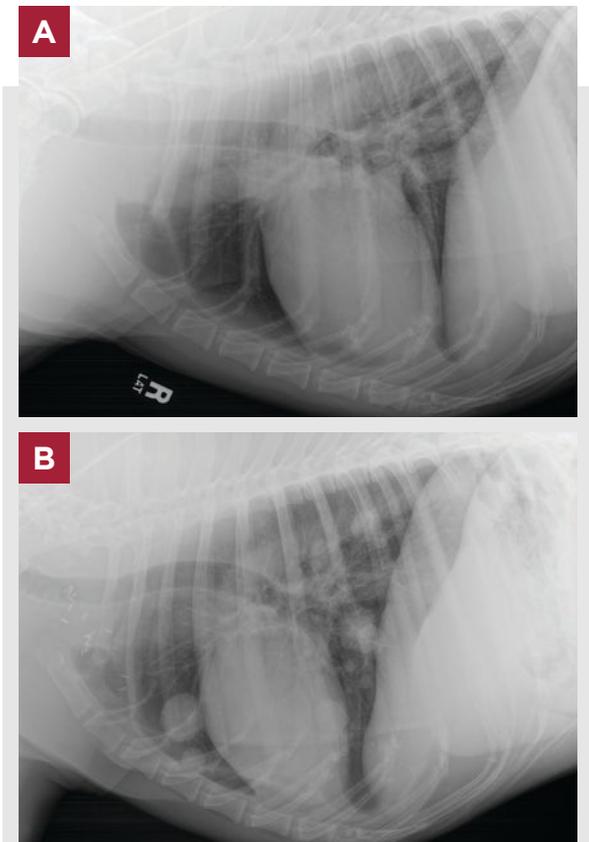


FIGURE 3. (A) Normal right lateral thoracic radiograph of a dog. **(B)** Right lateral thoracic radiograph of a dog with metastatic pulmonary nodules.



nodules are noted throughout the lungs that appear consistent with metastatic disease. Oral melanoma becomes a diagnostic differential, as it is more likely to metastasize to the lungs than squamous cell carcinoma. In a real-life example, **FIGURE 4** is a thoracic radiograph obtained in a 16-year-old cat as part of staging diagnosed intestinal lymphoma. The radiograph shows a primary pulmonary tumor.

Ultrasonography

While the outlines of masses can be seen on radiographs, ultrasonography provides a detailed look at organs and lymph nodes. Masses in the caudal half of the body often drain into lymph nodes within the abdominal cavity, and abdominal ultrasonography allows visualization of changes as well as safe sampling by needle or biopsy of the affected organ. Fluid can also be safely sampled to look for cancer cells or confirm hemoabdomen.

Thoracic ultrasonography can be used to view the heart to confirm if a mass noted on radiographs is heart based. It can also be used to visualize pulmonary masses, to guide aspiration, or to determine whether a process is benign or malignant or whether a tumor is primary or metastatic.¹¹

Ultrasonography can also be used on solitary tumors. When performing aspiration, the clinician needs to obtain cells from the tumor itself, not from potential pockets of fluid within the mass. For cavitory masses, ultrasonography can identify the best aspiration location.

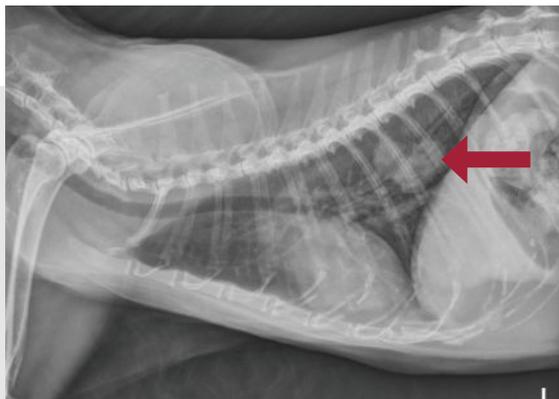


FIGURE 4. Right lateral thoracic radiograph of a cat with a pulmonary mass identified (**red arrow**).

Computed Tomography

Over the past several years, CT has become faster and more accessible, and its imaging capabilities have improved. CT is one of the most sensitive imaging modalities readily available to detect metastasis and extent of a primary tumor. It can be used to scan for lung nodules, abdominal organ changes, or bony changes associated with the tumor or spread.¹² It is often used to visualize the extent of invasion of oral and nasal tumors into surrounding bones or through the cribriform plate (**FIGURE 5**). The need for general anesthesia can be cost prohibitive; however, if a patient is already under general anesthesia, thoracic or abdominal CT may be added to detect metastasis instead of radiography and/or ultrasonography. Many CT scans can now be performed with the patient under heavy sedation, making them more accessible to the average pet owner.

Magnetic Resonance Imaging

MRI is not as useful in veterinary medicine as in



FIGURE 5. (A) Normal computed tomography (CT) scan slice of a feline skull. (B) CT scan slice of a feline skull showing destruction of the nasal turbinates and infiltration of a tumor.

human medicine due to its limited availability and high cost. It is primarily used to image brain tumors. The detail aids in treatment planning and determining whether surgical removal is possible. As veterinary MRI develops and becomes more accessible, whole-body scans could be considered in lymphoma staging to more accurately image all organ systems and determine the presence of neoplastic processes.¹³

COMMON CANCERS AND STAGING PROTOCOLS

Regardless of cancer type, a serum biochemistry panel, CBC, and urinalysis are recommended as part of every cancer staging protocol to complete the health profile. Specific imaging and cytology tests are recommended based on cancer type (**TABLE 1**). The trifecta of common staging tests is aspiration, thoracic radiography, and abdominal ultrasonography.

Lymphoma

As the most common veterinary cancer, lymphoma has the simplest staging system to remember. Because there are lymph vessels throughout the body, lymphoma can develop anywhere; therefore, staging includes all diagnostic tests. A diagnosis can be made from cytology. Abnormal laboratory findings can include hypercalcemia, elevations in hepatic and renal values, and anemia. Imaging includes 3-view thoracic radiographs and abdominal ultrasonography, which may show sternal and abdominal lymphadenopathy, a mediastinal mass, or changes to any abdominal organ, including the spleen, liver, kidney, and urinary tract. Abnormal findings should be aspirated for confirmation. Additional testing includes bone marrow aspiration and immunophenotyping. The most common stage seen in dogs is stage IIIa—generalized peripheral lymphadenopathy without systemic signs.¹ This system is used almost exclusively for dogs as cats tend to be diagnosed with small cell lymphoma, which does not follow the same pattern.¹⁴

Mast Cell Tumors

MCTs can be found in both cats and dogs, but they are more common in dogs. While MCTs do not normally metastasize to the lungs, 3-view thoracic radiographs help complete the health profile. Lymphadenopathy of sternal lymph nodes may also be seen on radiographs of patients with MCTs on the thoracic half of the body. Imaging includes abdominal ultrasonography. Any



Regardless of cancer type, a serum biochemistry panel, CBC, and urinalysis are recommended as part of every cancer staging protocol to complete the health profile.

abdominal abnormalities should be aspirated. Because MCTs spread to the lymphatic system, aspiration should be performed on the local lymph node and spleen, even if they appear normal. The patient should be thoroughly examined for any additional masses, and all should be aspirated and noted on a body map.¹⁰

Melanoma

Malignant melanoma is a common and serious skin cancer. While it can develop in many locations, it is the most common oral malignancy in dogs. It is often locally aggressive and metastasizes readily to the lungs and local lymph nodes. Imaging includes thoracic radiographs and abdominal ultrasonography. While it is rare for melanoma to spread to internal organs, lymph node abnormalities can be noted depending on the location of the primary tumor.^{15,16}

With oral or ocular tumors, a CT scan is also warranted to evaluate the extent of the tumor. A full-body scan can be performed in lieu of radiographs and ultrasonography if a CT scan is recommended and the patient will already be anesthetized. Local lymph nodes should be aspirated if possible, even without lymphadenopathy. The submandibular lymph node can be removed at the same time as oral surgery and sent for histopathology to confirm involvement. Melanoma often requires additional treatment after surgery.^{15,16}

Osteosarcoma^{17,18}

Canine appendicular osteosarcoma is the most common form of osteosarcoma in veterinary medicine. Staging includes full bloodwork and thoracic radiographs. Elevations in alkaline phosphatase are common and have been associated with a poorer prognosis. Most osteosarcomas have metastasized by



the time they are diagnosed. If no metastasis is seen on radiographs, a CT scan could be performed at the time of surgery, as it is more sensitive than radiographs to micrometastasis. Aspiration of the local lymph node can be performed before surgery, but in cases of rear limb amputation, histopathology of the local lymph node is usually performed.

Hemangiosarcoma

There are several types of hemangiosarcoma,¹⁹ and not all are serious. Most veterinary nurses are familiar with splenic hemangiosarcoma, which can lead to hemoabdomen. When a patient presents with hemoabdomen, time is of the essence and the patient often will not survive without surgery. It is still important to take time to stage splenic hemangiosarcoma to allow clients to make an informed decision about whether to go to surgery. Lab work is required, and anemia is the most common abnormality. Obtaining the packed cell volume (PCV) of the peripheral blood and comparing it with the PCV of any abdominal effusion can help determine whether a mass is actively bleeding. Imaging should include both abdominal ultrasonography and 3-view thoracic radiographs. Hemangiosarcomas are most likely to metastasize to the liver and lungs and are visible as nodules or masses. Splenic hemangiosarcoma already carries a poor prognosis, and evidence of spread at the time of presentation can be the deciding factor between treatment and euthanasia.

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Danielle has worked for almost 20 years in veterinary medicine, with the last 14 in emergency and specialty practice. Her areas of special interest are oncologic pharmacology, specifically chemotherapy, and paraneoplastic syndromes. Her other passion is the people in veterinary medicine. She currently works as a regional training partner for BluePearl Veterinary Partners and focuses on training and career development for technicians and assistants. She is the current director-at-large for oncology in AIMVT and lectures nationally on various topics, including chemotherapy, grief, compassion fatigue, burnout, and communication.



CONCLUSION

Having a deeper understanding of the staging process can help the veterinary nursing staff feel more comfortable facing questions from clients and anticipating the doctor's needs. Much of what is used in veterinary oncology comes from advancements in human medicine, which may help in explaining tests and staging systems to clients. **TVN**

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CONTINUING EDUCATION

Staging Cancer: Digging Deeper Than the Diagnosis

ARTICLE OVERVIEW

This article describes why staging is an important step in cancer diagnosis and treatment, including the information that laboratory tests, cytology, histopathology, and imaging can provide.

LEARNING OBJECTIVES

After reading this article, participants will be able to define cancer staging with regard to diagnostic tests. Readers will be able to describe the staging tests, as well as identify appropriate staging procedures for common types of cancer.

This article has been submitted for **RACE approval for 1 hour of continuing education credit** and will be opened for enrollment when approval has been received. To receive credit, take the test for free by visiting [vetfolio.com](https://www.vetfolio.com) and entering the title of the article in the search bar. Free registration is required. Questions and answers online may differ from those below. Tests are valid for 2 years from the date of approval.

1. Which diagnostic test(s) is/are recommended as part of staging all oncology patients, regardless of type of cancer?
 - a. Serum biochemistry, complete blood count, and urinalysis
 - b. Fine needle aspiration
 - c. Thoracic radiography
 - d. Abdominal ultrasonography
2. True or false: All tumors metastasize to the lungs.
 - a. True
 - b. False
3. Which type of tumor can cause the paraneoplastic syndrome of polycythemia?
 - a. Liver
 - b. Pituitary
 - c. Renal
 - d. Splenic
4. Oral melanoma most commonly metastasizes to which 2 locations?
 - a. Brain and lungs
 - b. Lymph node and lungs
 - c. Tongue and lungs
 - d. Tongue and lymph node
5. True or false: The "N" in the TNM staging system stands for neoplasia.
 - a. True
 - b. False
6. Which imaging modality is most sensitive in detecting metastasis?
 - a. Computed tomography
 - b. Radiography
 - c. Ultrasonography
 - d. Magnetic resonance imaging
7. Which laboratory test gives very little staging information but is necessary to complete the patient's medical file?
 - a. Complete blood count
 - b. Immunophenotyping
 - c. Serum biochemistry
 - d. Urinalysis
8. Why should tumors be staged prior to surgical removal?
 - a. Metastasis automatically increases the patient's anesthetic risk.
 - b. Staging helps predict tumor aggressiveness.
 - c. Staging can determine treatment choices.
 - d. There is no need to stage a tumor if it is going to be surgically removed.
9. Dogs with lymphoma commonly present with no other signs other than peripheral lymphadenopathy. Which stage is this?
 - a. Stage IIb
 - b. Stage IIIa
 - c. Stage IVa
 - d. Stage Vb
10. True or false: The spleen can look normal on ultrasound despite the presence of mast cell tumor metastasis.
 - a. True
 - b. False