

2016 AAHA Oncology Guidelines  
for Dogs and Cats



# IMPLEMENTATION TOOLKIT





## Inside This Toolkit

Why Guidelines Matter.....	3
2016 AAHA Oncology Guidelines for Dogs and Cats.....	5
At-a-Glance Highlights .....	6
The Role of the General Practitioner or Referring Veterinarian.....	9
Making a Referral and Working with Specialists .....	10
Optimizing the Contributions of the Entire Practice Team.....	11
Safety Considerations for Personnel, Patients, Pet Owners, and the Environment.....	12
Safe Handling of Chemotherapy Drugs.....	15
Client Support and Communication.....	16
Bo: A Case Study on Canine Osteosarcoma.....	17
Chemotherapy Extravasation Management.....	19
AAHA's Resources on Oncology .....	22

## AAHA Standards of Accreditation

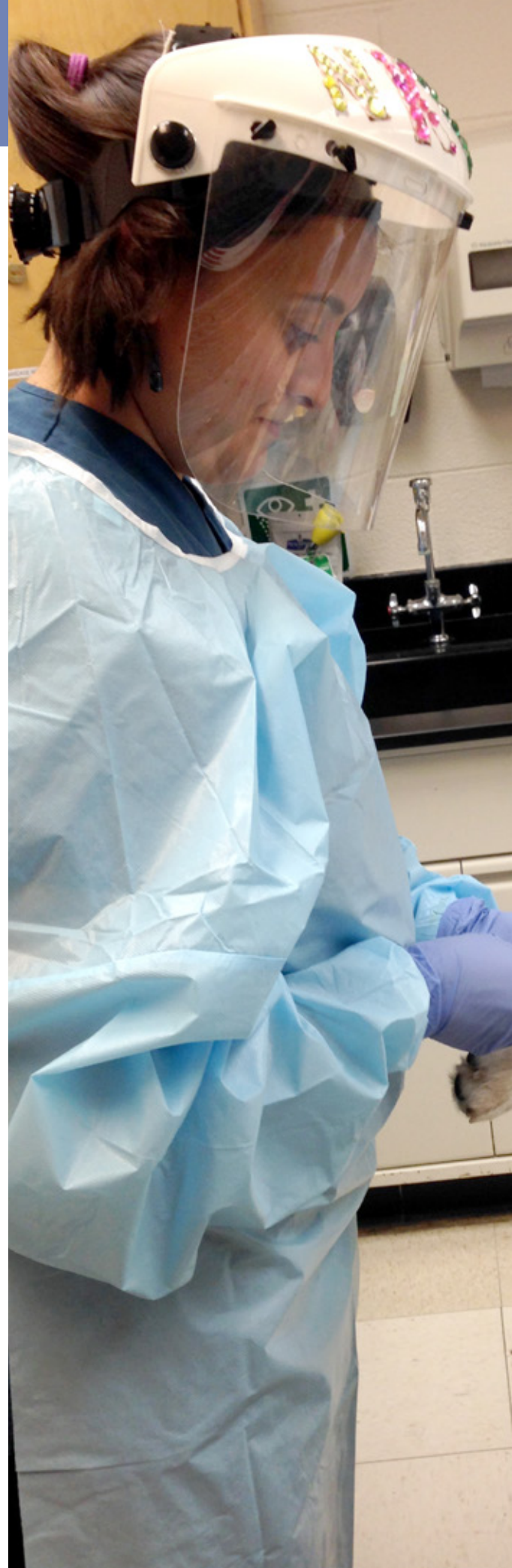
The *AAHA Standards of Accreditation* include standards that address oncology. For information on how accreditation can help your practice provide the best care possible to your patients, visit [aaha.org/accreditation](http://aaha.org/accreditation) or call 800-252-2242.

### Free web conference available August 22–September 18

Join Barb Biller, DVM, PhD, DACVIM (oncology), and John Berg, DVM, MS, DACVS, for an engaging discussion on best practices for veterinary staff to implement the *2016 AAHA Oncology Guidelines for Dogs and Cats*.

Earn 1 hour of CE credit.

**For more information and to register,  
go to [aaha.org/webconf](http://aaha.org/webconf)**



Veterinary practice guidelines, including the *2016 AAHA Oncology Guidelines for Dogs and Cats*, help ensure that pets get the best possible care. From medical director to veterinary assistant, guidelines keep your hospital staff on the cutting edge of veterinary medicine.

The *2016 AAHA Oncology Guidelines for Dogs and Cats* is a complete and medically sound compilation of updates, insights, advice, and recommendations for an oncology diagnosis and treatment. These guidelines help ensure all pets have the benefits of correct diagnosis and management of their cancer to maintain the best quality of life possible throughout their lifetime.

AAHA guidelines review the latest information to help veterinary staff address central issues and perform essential tasks to improve the health of the pet. In addition, AAHA guidelines define the role of each staff member so that everyone on the healthcare team can work together to offer the best-quality medical care.

Guidelines are just that: a guide established by experts in a particular area of veterinary medicine. Guidelines do not outweigh the veterinarian's clinical judgment; instead, AAHA guidelines help veterinarians develop and carry out treatment plans that meet each patient's individual needs and circumstances.

Aligning your practice's protocols with AAHA guideline recommendations is a key step in ensuring that your practice continues to deliver best-quality care. To support your dedicated efforts, AAHA is pleased to offer this toolkit. Here you will find facts, figures, highlights, tips, client and staff handouts, and other tools you can use every day to implement the recommendations of the *2016 AAHA Oncology Guidelines for Dogs and Cats*.

Thank you for helping to advance our shared mission to deliver the best in companion animal medical care. Together, we can make a difference!

*Michael T. Cavanaugh, DVM*

Michael T. Cavanaugh, DVM, DABVP (C/F)  
AAHA Chief Executive Officer

---

When selecting products, veterinarians have a choice of those formulated for humans and those developed and approved for veterinary use. Manufacturers of veterinary-specific products spend resources to have their products reviewed and approved by the US Food and Drug Administration (FDA) for use in canines and/or felines. These products are specifically designed and formulated for dogs and cats; they are not human generic products. AAHA suggests that veterinary professionals make every effort to use veterinary FDA-approved products when available and base their inventory purchasing decisions on what product is most beneficial to their patients.

---

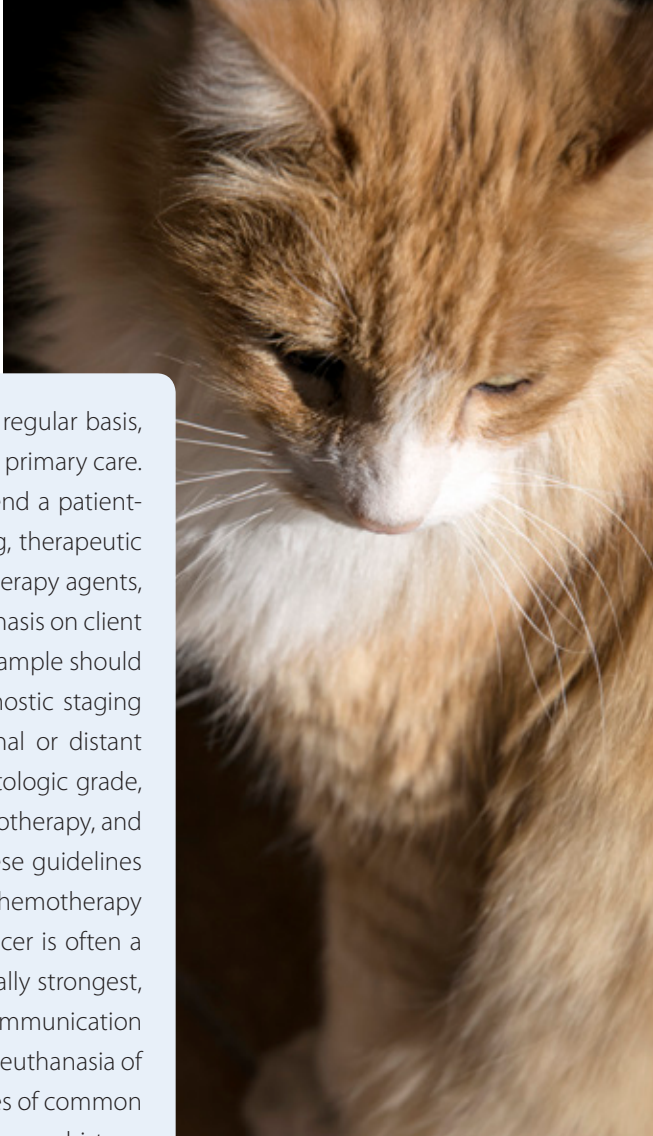


# 2016 AAHA Oncology Guidelines for Dogs and Cats\*

Barb Biller, DVM, PhD, DACVIM (oncology), John Berg, DVM, MS, DACVS, Laura Garrett, DVM, DACVIM (oncology), David Ruslander, DVM, DACVIM (oncology), DACVR, Richard Wearing, DVM, DABVP, Bonnie Abbott, DVM, Mithun Patel, PharmD, Diana Smith, BS, CVT, Christine Bryan, DVM

## Abstract

All companion animal practices will be presented with oncology cases on a regular basis, making diagnosis and treatment of cancer an essential part of comprehensive primary care. Because each oncology case is medically unique, these guidelines recommend a patient-specific approach consisting of the following components: diagnosis, staging, therapeutic intervention, provisions for patient and personnel safety in handling chemotherapy agents, referral to an oncology specialty practice when appropriate, and a strong emphasis on client support. Determination of tumor type by histologic examination of a biopsy sample should be the basis for all subsequent steps in oncology case management. Diagnostic staging determines the extent of local disease and presence or absence of regional or distant metastasis. The choice of therapeutic modalities is based on tumor type, histologic grade, and stage, and may include surgery, radiation therapy, chemotherapy, immunotherapy, and adjunctive therapies, such as nutritional support and pain management. These guidelines discuss the strict safety precautions that should be observed in handling chemotherapy agents, which are now commonly used in veterinary oncology. Because cancer is often a disease of older pets, the time of life when the pet-owner relationship is usually strongest, a satisfying outcome for all parties involved is highly dependent on good communication between the entire healthcare team and the client, particularly when death or euthanasia of the patient is being considered. These guidelines include comprehensive tables of common canine and feline cancers as a resource for case management and a sample case history. (*J Am Anim Hosp Assoc* 2016; 52:181–204. DOI 10.5326/JAAHA-MS-6570)



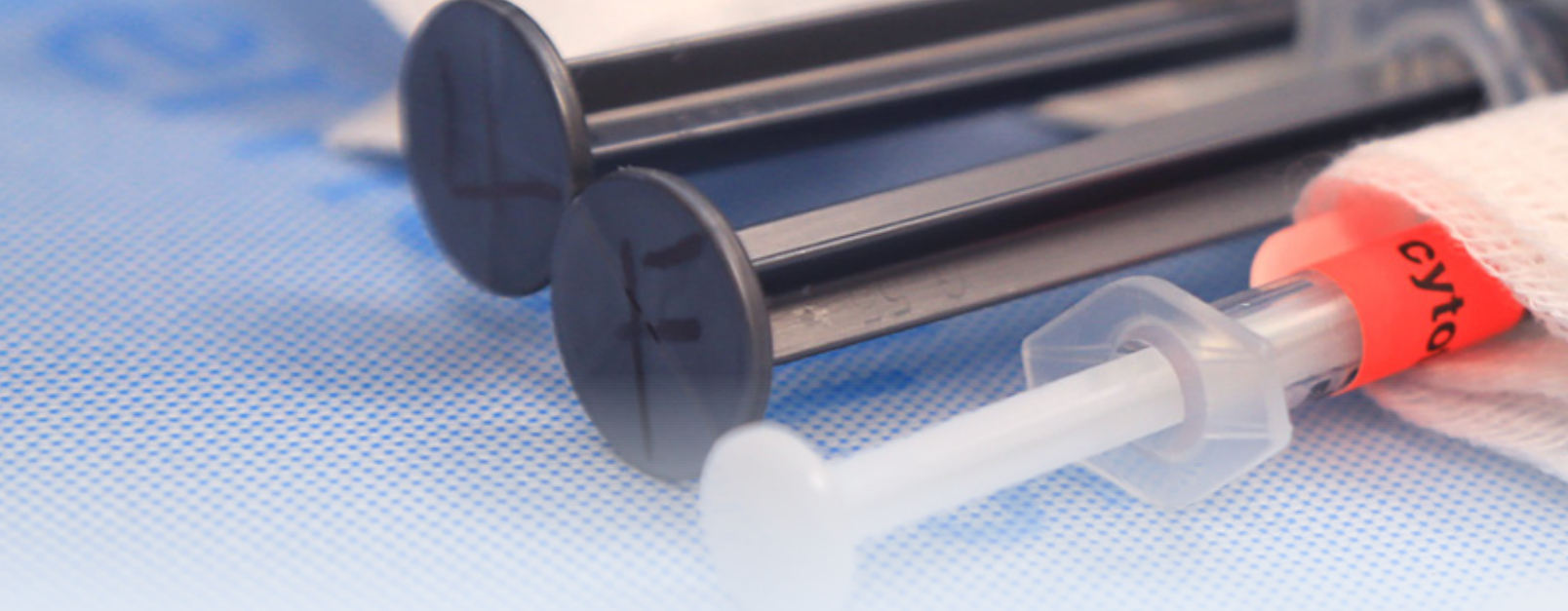
 **To access the complete version of the guidelines document including the references and tables, please refer to the 2016 AAHA Oncology Guidelines for Dogs and Cats and find a downloadable version of tables listing common tumors of dogs and cats at [aaha.org/oncology\\_guidelines](http://aaha.org/oncology_guidelines).**

From Flint Animal Cancer Center, College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins, CO (B.B.); the Department of Clinical Sciences, Foster Hospital for Small Animals, Cummings School of Veterinary Medicine, Tufts University, North Grafton, MA (J.B.); College of Veterinary Medicine at Illinois, University of Illinois at Urbana-Champaign, Urbana, IL (L.G.); Veterinary Specialty Hospital of the Carolinas, NC (D.R.); VCA Ragland & Riley Animal Hospital, Livingston, TN (R.W.); Arapahoe Animal Hospital, Boulder, CO (B.A.); College of Veterinary Medicine, North Carolina State University, Raleigh–Durham, NC (M.P.); Red Bank Veterinary Hospital, NJ (D.S.); and Department of Clinical Sciences, College of Veterinary Medicine, Mississippi State University, Starkville, MS, and Primary Care Veterinary Educators (C.B.).

Correspondence: [john.berg@tufts.edu](mailto:john.berg@tufts.edu) (J.B.)

ALP (alkaline phosphatase); ASTM (American Society for Testing and Materials); BSC (biological safety cabinet); CSTD (closed system transfer devices); CT (computed tomography); FNA (fine-needle aspiration); HD (hazardous drug); MTD (maximally tolerated dose); NIOSH (National Institute for Occupational Safety and Health); NSAID (nonsteroidal anti-inflammatory drug); PPE (personal protective equipment); TKI (tyrosine kinase inhibitor); USP (United States Pharmacopeia)

\*These guidelines were prepared by a task force of experts convened by the American Animal Hospital Association for the express purpose of producing this article. They were subjected to the same external review process as all *JAAHA* articles. This document is intended as a guideline only. Evidence-based support for specific recommendations has been cited whenever possible and appropriate. Other recommendations are based on practical clinical experience and a consensus of expert opinion. Further research is needed to document some of these recommendations. Because each case is different, veterinarians must base their decisions and actions on the best available scientific evidence, in conjunction with their own expertise, knowledge, and experience. These guidelines were supported by a generous educational grant from Aratana Therapeutics, Medtronic, and Zoetis.



## At-a-Glance Highlights

**Oncology cases are inevitable in clinical practice**, therefore some degree of expertise in the diagnosis and treatment of cancer is expected by clients and is an essential component of a comprehensive primary care veterinary practice.

**Because oncology patients are frequently of an advanced age, their owners are often highly bonded to them** and emotionally distraught after receiving a cancer diagnosis.

**Referral of an oncology patient is a multifactorial process** that considers the patient's quality of life and the pet owner's preferences, emotional attachment to the animal, and the adequacy of his or her physical and financial resources to properly care for the animal.

**The primary care clinician, specialist, and pet owner must work together** as a unified healthcare team and have a shared understanding of the options, procedures, and expectations of referral treatment.

**Once the possibility of a neoplastic process is suspected**, determination of the tumor type serves as the basis for all subsequent steps in patient management.

**A biopsy is the basic tool that allows removal and examination of cells** from the body to determine the presence, cause, or extent of a disease process.


**Fine-needle sampling, which may or may not involve aspiration, can be performed safely** for the majority of external tumors, without sedation or anesthesia.

**With training and experience, the general practitioner can often determine the presence and type of neoplasia in the office.** Submission to a clinical pathologist for diagnostic confirmation is usually indicated prior to therapy.

**Diagnostic staging is a mainstay of oncology case management.** Staging is the process of determining the extent of local disease and the presence or absence of regional or distant metastasis.

**Chemotherapy is now a commonly used treatment modality** in veterinary cancer medicine.

**Adjunctive therapies have long been used** as a means of improving the quality of life in veterinary cancer patients and are now an accepted component of oncology case management.



**The nutritional status of all oncology patients should be routinely assessed** beginning at diagnosis and throughout treatment.

**Recognition and alleviation of pain in oncology patients** is essential for maintaining quality of life.

**In simple terms, radiation therapy utilizes ionizing radiation to kill cancer cells.**

**Palliative radiation is playing a larger role in veterinary oncology** as owners increasingly seek to improve quality of life, decrease pain, and minimize hospitalization of their pets rather than achieve a cure.

**As a general rule, if a primary tumor can be completely excised with acceptable morbidity, surgery is the best choice of treatment.** The first attempt at surgical excision always offers the best opportunity to completely remove the tumor.

**All excised tumors should be submitted** for histopathologic examination and margin analysis.

**The importance of attention to appropriate safety precautions in handling hazardous drug (HD) preparations in the hospital setting cannot be overemphasized.** The veterinarian is legally and ethically obligated to educate staff regarding safe handling of chemotherapeutic drugs.

**Errors in dose calculations are responsible for a large portion of mistakes made in chemotherapy.** Chemotherapeutic agents have a narrow therapeutic index and can lead to significant or fatal toxicity if overdosed.

**Multiple studies in human oncology confirm that effective communication skills are a critical source of satisfactory case outcome** for both the patient and clinician.

**It is important to enlist the skills and resources of the entire healthcare team** when caring for an oncology patient.

**Because oncology cases may conclude with the death or euthanasia of the patient,** a satisfying outcome for all is highly dependent on good communication between the practitioner and the client.





# The Role of the General Practitioner or Referring Veterinarian

Managing oncology cases requires special equipment, supplies, and training. While some general practitioners feel comfortable treating cancer, others may prefer not to provide chemotherapy, and few will have access to radiation therapy without referral. In most cases, however, it is the general practitioner who makes the diagnosis of neoplasia and breaks the news to the pet owner.

The referring veterinarian's role varies depending on several factors, such as the cancer type, treatment plan, treatment modalities, client's proximity to the specialist, and the referring veterinarian's comfort level with the disease process and treatment. The following list, though not exhaustive, highlights the responsibilities of the general practitioner following the diagnosis:

## Getting Started

- Deliver the diagnosis with empathy to the owner (see full discussion in the full version of the guidelines).
- Stage the disease and form a prognosis.
- Create an initial treatment plan.
- Meet with the owner to discuss the prognosis, recommended treatment, and the pet owner's preferences.
- Discuss with the pet owner the need or desire for referral to a specialist.

## Referring the Patient

- Communicate with the referral specialists, including, but not limited to, oncologists, surgeons, internists, and radiologists.
- Consult the specialty practice(s) to determine what patient information they require. The information required varies depending upon the specialist, the case, and the patient.
- Compile a complete copy of the patient's medical records to make available to the specialist, including
  - Description of current disease process
  - Previous medical history
  - Cytology/fine-needle aspirate results
  - Histopathology reports
  - Lab work (blood work and urinalysis)
  - Radiographs
  - Current medications
- Consult with the specialty practice(s) to select a preferred method of communication: phone, email, or other.

- Educate staff about the referral process and all aspects of working with a specialist, for example, preferred method of communication and sharing medical records.
- Educate staff about the patient's cancer, including diagnosis, treatment, prognosis, disease progression, and the reasons for referring the case.

## Developing the Treatment Plan

- After the specialist sees the patient, develop a treatment plan. The treatment plan may be created by the specialist, the referring veterinarian, or both.

## Providing Treatment

- The referring veterinarian's responsibilities depend on the treatment plan. The referring veterinarian may
  - Provide all care.
  - Perform monitoring lab work during chemotherapy protocols, for example, serum chemistry, urinalysis, or weekly CBC tests, and send results to the specialist.
  - Perform surgical procedures (for example, amputation).
  - Monitor and assess surgical sites as well as postsurgical complications.
  - Administer all or some doses of chemotherapy.
  - Dispense medications (antibiotics, anti-emetics, nutritional supplements, gastrointestinal protectants, etc.) as prescribed by the specialist or as necessary due to side effects or complications.
  - Perform serial radiographs to monitor disease and/or metastatic progression.
- Provide hospice care.

## Communicating

- Support owners through the process, even if the referring veterinarian is not directly involved in treating the patient.
- Maintain communications among the general practice and referring veterinarian, specialty practice(s) and specialists, and client.



Referrals are appropriate when the primary care clinician can no longer meet the needs and expectations of the patient and client.

## Making a Referral and Working with Specialists

Practitioners who refer an oncology patient to a specialist should be mindful of the following considerations:

- Each patient and case is unique.
- Referral of an oncology patient is a multifactorial process that considers the patient's quality of life (pre- and post-referral) and the pet owner's preferences, emotional attachment to the animal, and the adequacy of his or her physical and financial resources to properly care for the animal.
- The primary care clinician, specialist, and pet owner must work together as a unified healthcare team and have a shared understanding of the options, procedures, and expectations of referral treatment.
- Aside from maximizing the patient's survival, all parties involved in referral decisions should focus on the patient's quality of life and the importance of providing compassionate, empathetic support for the owner.

Referral of an oncology patient may be appropriate for a variety of reasons. These include when the primary care veterinarian or the client wishes to consider all possible treatment options or when the referring veterinarian cannot provide optimum treatment for any reason. In addition, specialty referral practices often have access to clinical trials in which the client may want to participate.

Referral to a specialist should be case-specific. Referrals are appropriate when the primary care clinician can no longer meet the needs and expectations of the patient and client. The comfort level of the primary clinician and client with referral treatment will dictate how early in the process case transfer should occur. The importance of a clear, shared understanding of the referral process by the pet owner, primary care veterinarian, and specific referral specialists or referral centers cannot be overemphasized. Determination of the preferred method of collaboration and case transfer between the primary care clinician and specialist should be made in advance of the referral treatment.

For more information about working with referral specialists, see the *2013 AAHA Referral Guidelines*, [aaha.org/referral\\_guidelines](http://aaha.org/referral_guidelines).





## Optimizing the Contributions of the Entire Practice Team

It is important to enlist the skills and resources of the entire healthcare team when caring for an oncology patient. Good communication and understanding of the practice's oncology protocols within the team allow each member to provide the client with consistent information on the patient's status, treatment plan, and outcomes. By "speaking with one voice," the practice minimizes the potential for confusion and disillusionment of the client when an often sensitive oncology case is involved. An informed, empathetic team approach to presenting information empowers the client to make an educated decision on treatment options and helps create realistic expectations for treatment outcome, quality of life, and life expectancy.

### **The Critical Role of Staff Training**

The entire healthcare team can contribute in a unified fashion to managing an oncology patient and supporting its owner. To accomplish this, a thoughtful approach must be taken to defining the roles and responsibilities of each staff member involved in an oncology case. Equally important, if not more so, is to conduct training to ensure that all staff members understand their responsibilities in such cases and have the skills and knowledge to carry them out. In particular, staff training is most effective when it addresses empathetic interaction with pet owners and safe handling of chemotherapy drugs. An expectation that all staff members will effectively contribute to oncology case management is not realistic unless they have been trained to do so. Practices should assess their training programs to ensure that the unique requirements of oncology treatment are specifically addressed.

Useful recommendations for engaging and training the entire healthcare team to implement clinical protocols are provided in recently published feline healthcare guidelines.

### **Challenges and Fulfillment for the Healthcare Team**

Cancer treatment can be emotionally difficult for all concerned. For example, compassion fatigue is a phenomenon characterized by a gradual decline in interest and empathy toward individuals experiencing hardship. Compassion fatigue is real and can negatively impact the quality of care. Body language that conveys impatience, superficial interest, or false sincerity is readily perceived by the client. A team approach to oncology case management is an excellent way to combat compassion fatigue affecting an individual member. When each member of the team supports and complements each other, compassion fatigue is less likely to occur in the first place and other negative behavior patterns can be detected and discussed among the staff.

The opportunity to demonstrate compassionate care and possibly extend the life of a valued pet while offering empathy for its owner can make oncology cases some of the most fulfilling a veterinarian and the entire practice team will encounter. Treatment of a cancer patient is especially rewarding when the outcome is remission or cure, improved quality of life, or longer lifespan for the patient. Even in cases where a favorable outcome does not occur, the experience can still leave the client with a positive impression of the practice. This occurs when the healthcare team is perceived as united in its commitment to the patient's welfare and genuinely concerned about the relationship between the pet and its owner.

# Safety Considerations for Personnel, Patients, Pet Owners, and the Environment

The importance of attention to appropriate safety precautions in handling hazardous drug (HD) preparations in the clinic setting cannot be overemphasized. The veterinarian is legally and ethically obligated to educate staff regarding safe handling of chemotherapeutic drugs. Lack of staff communication and training in chemotherapy protocols could lead to an Occupational Safety and Health Administration investigation, fines, and lawsuits. Staff should have access to relevant Safety Data Sheets and be made aware of the toxicity of any chemotherapeutic agent that is used in the practice.

For the purposes of these guidelines, HDs will be used interchangeably with chemotherapeutic agents. A complete list of HDs has been compiled by the Centers for Disease Control and Prevention and the National Institute for Occupational Safety and Health (NIOSH). Improper handling can lead to unintended exposure to cytotoxic agents that are mutagenic, teratogenic, or carcinogenic. For example, exposure of healthcare workers to HDs has been confirmed by the presence of HD metabolites in urine. For this reason, safety is a paramount consideration for everyone involved with chemotherapy.

## Personnel Safety Considerations

There are several routes of exposure to HDs. HDs can enter the body via inhalation, accidental injection, ingestion of contaminated foodstuffs, hand-to-oral contact, and dermal absorption. While HD exposure is always a constant threat when chemotherapeutic agents are used, proper procedures and policies can minimize the risk. The United States Pharmacopeia (USP) has developed an enforceable “General Chapter” practice standard devoted to the handling of HDs, which outlines standards regarding personnel protection for preparation and handling of HDs. Because an in-depth discussion of HD controls is beyond the scope of these guidelines, readers can refer to USP for more detailed information on this topic.

Veterinary practices will ordinarily not be involved in chemotherapeutic drug compounding. However, it is helpful for the healthcare team personnel to have a general awareness that direct contact with HDs, either by handling, reconstituting, or administering HDs, represents an exposure risk. Many HDs have also been found to have drug residue on the outside of drug containers, which creates another opportunity for exposure of individuals who receive drugs and perform inventory control procedures. Personal protective equipment (PPE) should be used to protect personnel from exposure during handling of HDs. PPE includes gloves, gowns, goggles for eye protection, a full face shield for head protection, and respiratory barrier protection.

Regular exam gloves are not recommended for use as standard protocol for handling chemotherapeutic agents. However, as an expedient, wearing two pairs of powder-free nitrile or latex gloves can be used as a last resort. Vinyl gloves do not provide protection against chemotherapy. Ideally, gloves should be powder free and rated for chemotherapy use by the American Society for Testing and Materials (ASTM). For receiving HDs, one pair of ASTM-tested chemotherapy gloves may be worn. When administering, managing, and disposing of HDs, two pairs of ASTM-tested chemotherapy gloves may be worn. The inner glove should be worn under the gown cuff and the outer glove over the cuff. Disposable gowns made of polyethylene-coated polypropylene or other laminate materials offer the best protection.

Eye, face, and respiratory protection is mandatory when working with HDs outside of a clean room or isolator cabinet, or whenever there is a probability of splashing or uncontrolled aerosolization of HDs. A full face mask is a suitable alternative to goggles, although it does not form a seal or fully protect the eyes. A NIOSH N95 respirator mask is suitable for most situations, with the exception of large spills that cannot be contained by a commercially available spill kit.

PPE should be removed in the following order:

1. chemotherapy gown (touching the outside of the gown, then rolling the outside inward to contain HD trace contamination),
2. goggles and face shields (touching only the outside without making contact with the face),
3. chemotherapy gloves (touching the outside of the gloves away from the exposed skin while attempting to roll the glove outside-in).

If a glove becomes contaminated or if there is a breach in the glove, it should be removed and discarded promptly, while carefully avoiding contamination of the handler’s skin or nearby surfaces.

Closed-system transfer devices (CSTDs) are another type of PPE that can be used for any cytotoxic chemotherapy agent (although not necessarily for all HDs) during preparation and administration. In the case of non-cytotoxic agents that are not on the NIOSH list of HDs, for example, asparaginase, a CSTD, is not required. FDA approval of CSTDs requires the following capabilities: no escape of HDs or vapor, no transfer of environmental contaminants, and the ability to block microbial ingress. CSTDs can greatly reduce the potential for HD exposure to clinical personnel and should always be used concurrently with other PPE.

Traditional needle and syringe techniques for mixing HDs create the potential for droplet or aerosol contamination. CSTDs

prevent mechanical transfer of external contaminants and prevent harmful aerosols that are created by mixing HDs from escaping and exposing personnel. CSTDs are commercially available from a number of companies.

The following additional safety precautions will help minimize the potential for exposure of personnel handling HDs:

- Male and female employees who are immunocompromised or attempting to conceive and women who are pregnant or breastfeeding should avoid working with chemotherapy agents.
- Employees or pet owners who will be exposed to the patient's waste (urine, feces, vomit, blood) within 72 hr of chemotherapy administration (sometimes longer for some drugs) should wear proper PPE.
- Chemotherapy pills (tablets and capsules) are best handled within a biological safety cabinet (BSC) if available. If no BSC is available, a ventilated area or a respirator should be used to avoid inhalation of HD particles or aerosols.
- Separate pill counters should be used for chemotherapy pills. Counters labeled for chemotherapy use will help avoid inadvertent use with conventional medications. The counters should be stored either within the BSC (not to be removed) or in a sealed container (e.g., a plastic box with a secure lid) dedicated to that pill counter and any other items that may come in contact with HD pills.

### Environmental Safety Considerations

Environmental controls are an important part of risk mitigation. The recommended location for chemotherapy preparation and administration is a quiet, low-traffic room that is dedicated to chemotherapy purposes, free from distractions, and easy to clean. Because HD spill events represent the greatest risk of personnel exposure, it is important to use extreme care when cleaning spills. Commercially available spill kits are useful in containing and cleaning HD spills. Absorbent pads or pillows can be used to immediately contain larger spills. When managing a spill, it is recommended to start from the outer edges of the spill and work your way toward the middle to prevent spreading HD residue. An HD-spill management sequence (Table 4, see the full guidelines) has been developed and is a suitable basis for a veterinary practice protocol. Spill kits should contain instructions for use and be located in areas where HDs are located and administered. Only trained personnel should clean up HD spills, and they should wear appropriate PPE, including double chemotherapy gloves and respiratory masks. HD agents are best stored in a dedicated, closeable cabinet or refrigerator. Following administration, discard HDs, administration materials, and gloves and other PPE into chemotherapy waste receptacles. It is important that staff members who have touched chemotherapy vials or potentially contaminated areas NOT touch anything or anyone else until they have removed their PPE and washed their hands.



### Patient Safety Considerations

Chemotherapeutic agents have a narrow therapeutic index and can lead to significant or fatal toxicity if overdosed. Errors in dose calculations and labeling as well as breed-specific sensitivities can lead to adverse events. Errors in dose calculations are responsible for a large portion of mistakes made in chemotherapy. In veterinary medicine, agents may be dosed in terms of milligrams/kilogram (mg/kg) or milligrams per meter squared (mg/m<sup>2</sup>). These are easily confused and can lead to drastically different dose calculations. Prior to mixing chemotherapy drugs, calculations should be done by two individuals. The two calculated doses can then be compared and serve as a double check. The concentration of drug in mg/ml should also be double-checked.

The Washington State University College of Veterinary Medicine has extensively investigated the ABCB-1 gene (formerly known as MDR1), which is responsible for breed-specific variability in susceptibility to adverse events. The ABCB-1 gene codes for the production of p-glycoprotein (Pgp) pumps, which act to remove drugs from individual cells. The Washington State University College of Veterinary Medicine has published a list of breeds that have a high probability of an ABCB-1 gene mutation (Table 5, see the full guidelines). Many chemotherapy drugs, notably vincristine and vinblastine, are substrates for Pgp pumps and require a dose adjustment for that reason.

When administering chemotherapy to an animal, proper restraint is very important in order to prevent drug extravasation. Staff members assisting with restraint should wear chemotherapy gloves and other appropriate PPE. Frequent monitoring of the injection site should be performed throughout the injection or infusion. Placement of a small-gauge IV catheter (e.g., 24 g, 22 g) will preserve vein viability and provide secure access. Although



All HDs should be labeled clearly with chemotherapy warning labels.

winged infusion sets are not as secure as IV catheters, they can be used for bolus injections of drugs such as vinca alkaloids, cyclophosphamide, and carboplatin. Winged infusion sets should never be used for severe vesicants, such as doxorubicin, or for lengthy infusions.

Venipuncture should entail a nicely seated, one-stick technique in order to avoid creating multiple holes within the vein wall that would allow the chemotherapy drug to leak into surrounding tissue. After chemotherapy administration is complete, apply gauze or an alcohol swab to the injection site when removing the needle or catheter from the patient. This can help stabilize sudden movements of the exiting cannula as well as absorb possible residual chemotherapeutic agents contained within.

Because heparin can cause precipitation or inactivation of some chemotherapy agents, non-heparinized flushes are recommended. A 0.9% NaCl preparation is a standard fluid choice. Prime any lines with the 0.9% NaCl or other fluid prior to the addition or administration of chemotherapy.

### Extravasations

Extravasation is the process of liquid leaking into surrounding tissue, typically near the insertion site of a peripheral catheter. Drugs are classified according to their potential for causing damage as

vesicant, irritant, or a nonvesicant. Table 6 (see the full guidelines) lists the extravasation potential for five injectable chemotherapies used in veterinary medicine.

Most extravasation events can be prevented by a systematic, standardized, evidence-based approach to administration techniques. A trained and experienced staff will greatly decrease procedure-related extravasation risk factors. Fidalgo et al. outline a preventative protocol that may help minimize the risk of extravasations.

The most common signs of extravasation are discomfort, pain, swelling, and redness at the injection site. Prolonged symptoms often progress to tissue ulcerations, blistering, and necrosis. Indications of an extravasation event include the absence of blood return from the catheter, bolus administration resistance, and failure of the infusion. If an extravasation event does occur, do not immediately remove the catheter. Rather, attempt to aspirate as much drug as possible and do not inject any fluid into the catheter. An extravasation mitigation protocol should be implemented as soon as possible. (For more information on extravasations, see pp. 18–21.)

### Labeling of Hazardous Drugs

Labeling of HDs is an extremely important aspect of personnel safety. Without adequate HD labeling, personnel are placed at risk of accidental exposure to HDs. All HDs should be labeled clearly with chemotherapy warning labels. Injectable HD agents should be labeled as “opened” or “reconstituted” on a specific date and the concentration of the reconstituted agent should be indicated.

“Look-alike, sound-alike” describes drugs that are spelled and pronounced similarly but are different. The term came about in response to errors involving inadvertent misfills of drugs, for example, vincristine being confused with vinblastine. A simple practice that many pharmacies now follow is arranging their medication stock alphabetically by generic name using a “Tall Man Lettering System.” This is a simple way to emphasize spelling and pronunciation differences between drugs (e.g., vincristine is written as vinCRISTine and vinblastine is written as vinBLASTine).

Appropriate labeling of mixed chemotherapies can also reduce errors and allow for another double check prior to administration. Diluted drugs should be labeled with the amount of drug in milligrams contained in the syringe or minibag. For drugs that are not diluted, it is good practice to label the syringe with the concentration of the drug as it comes from the vial. These labeling techniques allow for another double check prior to administration.

The Institute for Safe Medical Practices has developed several strategies to prevent simple errors. Naked decimal points and trailing zeros have been implicated in many errors in healthcare and have been designated as unapproved abbreviations. An example of a naked decimal point is when “0.2 mg” is written as “.2 mg,” easily leading to a 10-fold overdose if “.2 mg” is read as “2 mg.” Similarly, a trailing zero notation is when “10 mg” is written as “10.0 mg,” which can easily be mistaken for “100 mg.”

# Safe Handling of Chemotherapy Drugs

**Direct contact with chemotherapy drugs (HDs)**, either by handling, reconstituting, or administering, represents an exposure risk.

**The recommended location** for chemotherapy preparation and administration is a quiet, low-traffic room that is dedicated to chemotherapy purposes, free from distractions, and easy to clean.

**Many HDs have also been found to have drug residue** on the outside of drug containers, which creates another opportunity for exposure of individuals who receive drugs and perform inventory control procedures.

**Personal protective equipment (PPE) should be used** to protect personnel from exposure during handling of HDs. PPE includes gloves, gowns, goggles for eye protection, a full face shield for head protection, and respiratory barrier protection.

**Regular exam gloves are not recommended** for use as standard protocol for handling chemotherapeutic agents. However, as an expedient, wearing two pairs of powder-free nitrile or latex gloves can be used as a last resort. Vinyl gloves do not provide protection against chemotherapy. Ideally, gloves should be powder free and rated for chemotherapy use by the American Society for Testing and Materials (ASTM). For receiving HDs, one pair of ASTM-tested chemotherapy gloves may be worn. When administering, managing, and disposing of HDs, two pairs of ASTM-tested chemotherapy gloves should be worn with the inner glove under the gown cuff and the outer glove over the cuff. If a glove becomes contaminated or if there is a breach in the glove, it should be removed and discarded promptly, while carefully avoiding contamination of the handler's skin or nearby surfaces.

**Disposable gowns** made of polyethylene-coated polypropylene or other laminate materials offer the best protection.

**Eye, face, and respiratory protection is mandatory** when working with HDs outside of a clean room or isolator cabinet, or whenever there is a probability of splashing or uncontrolled aerosolization of HDs. A full face mask is a suitable alternative to goggles, although it does not form a seal or fully protect the eyes. A NIOSH N95 respirator mask is suitable for most situations, with the exception of large spills that cannot be contained by a commercially available spill kit.

**PPE should be removed in the following order:** chemotherapy gown (touching the outside of the gown, then rolling the outside inward to contain HD trace contamination), goggles and face shields (touching only the outside without making contact with the face), then chemotherapy gloves (touching the outside of the gloves away from the exposed skin while attempting to roll the glove outside-in).

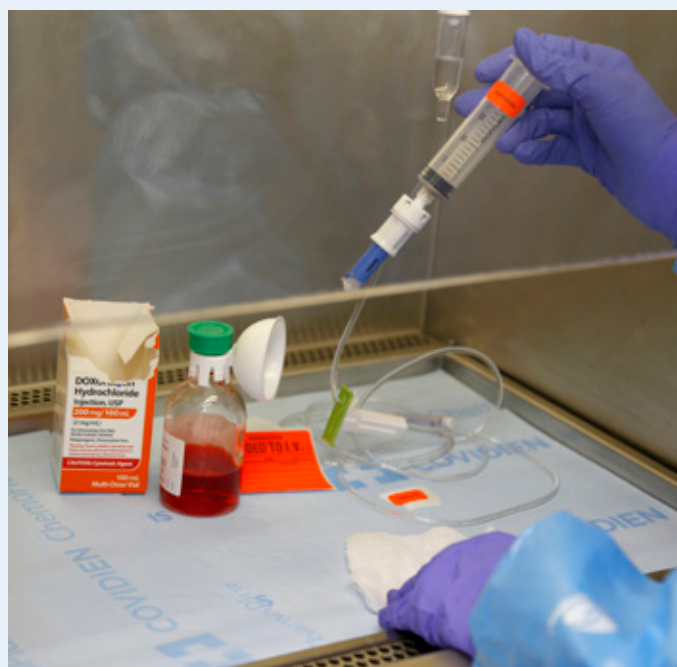
**Closed system transfer devices (CSTDs) are another type of PPE that can be used** for any cytotoxic chemotherapy agent (although not necessarily for all HDs) during preparation and administration. Traditional needle and syringe techniques for mixing HDs create the potential for droplet or aerosol contamination. CSTDs prevent mechanical transfer of external contaminants and prevent harmful aerosols that are created by mixing HDs from escaping and exposing personnel. CSTDs are commercially available from a number of companies.

**Male and female employees** who are immune-compromised or attempting to conceive and women who are pregnant or breastfeeding should avoid working with chemotherapy agents.

**Employees or pet owners** who will be exposed to the patient's waste (urine, feces, vomit, blood) within 72 hr of chemotherapy administration (sometimes longer for some drugs) should wear proper PPE.

**Chemotherapy pills (tablets and capsules) are best handled within a biological safety cabinet (BSC)** if available. If no BSC is available, a ventilated area or a respirator should be used to avoid inhalation of HD particles or aerosols.

**Separate pill counters should be used for chemotherapy pills.** Counters labeled for chemotherapy use will help avoid inadvertent use with conventional medications. The counters should be stored either within the BSC (not to be removed) or in a sealed container (e.g., a plastic box with a secure lid) dedicated to that pill counter and any other items that may come in contact with HD pills.



## Client Support and Communication

Good communication skills are a key component of a successful practice. Oncology cases raise the bar by placing a premium on the clinician's ability to engage and empathize with the owner of a cancer patient. Cancer is an upsetting diagnosis associated with emotionally charged situations. The goal of the initial discussion is to present detailed information about the diagnosis, testing and treatment options, and prognosis while at the same time assessing the client's goals and limitations, all done in an empathetic and supportive manner. Understanding costs, risks, benefits, and potential outcomes is crucial for owners of pets with cancer, as is feeling like part of a caring team battling the disease. Multiple studies in human oncology confirm that effective communication skills are a critical source of satisfactory case outcome for both the patient and clinician.

### Empathy

Empathy is the ability to imagine what a client is experiencing and to reflect that understanding. Stated another way, empathy can be thought of as having a client know that he or she is being seen, heard, and accepted. "You seem worried" or "you look like you have some questions" are statements that show clients that they are recognized as individuals with feelings and emotions, and not just as customers. While statements like these might seem awkward or unnatural at first, the ability to express empathy improves with practice. A common concern is that acknowledging a client's concerns or state of mind will escalate that person's emotions. Experts agree that the opposite usually occurs. Acknowledging their distress, discomfort, or doubts helps clients know that their feelings are seen and accepted. This usually helps the client focus on the medical discussion and treatment issues. Examples of nonverbal displays of empathy include varying your speaking tone and rate, adopting a sympathetic posture, or simply handing a box of tissues to a crying client.

To clients, knowing that they are being heard is as powerful as knowing they are seen and recognized. Telling clients that you recognize their concerns uses a core communication skill: reflective listening (discussed in more detail in the full guidelines). This type of acceptance will help the owner of a cancer patient to be open and express difficult or even embarrassing issues and questions. Statements like "I can see that this is difficult to discuss" or "it is common for these masses to be overlooked until they become large" can be reassuring to the client and open lines of discussion.

### Breaking the News

Clients need time to adjust to the idea that their pet may have cancer, particularly if the prognosis is poor. Being empathetic and candid in discussing a suspected or confirmed cancer diagnosis often helps the pet owner accept the situation and make treatment

decisions in a coherent, proactive manner. It is a good idea to announce a cancer diagnosis with a "warning shot" phrase, such as, "I'm afraid the news is not good." Using short phrases and waiting for the client's response is a good approach to discussing a cancer case. An example would be, "I'm so sorry about this upsetting diagnosis. Lymphoma is a common cancer in dogs. Unfortunately, it's not curable but the good news is that it is treatable." Then pause and ask, "Would you like to discuss further testing and treatment now, or would you prefer to talk later?"

Most clients will have a negative response to the words cancer and chemotherapy. Their initial reaction to a cancer diagnosis often changes as they process and accept the difficult news and listen to the options on how to proceed. It is not uncommon for an initial refusal to consider more testing or treatment to change with further discussion about how well most pets do with their therapy.

### Offering Options

When discussing a cancer diagnosis or treatment plan with a pet owner, it is important to use lay terminology or medical vocabulary accompanied by a clear explanation. Using clinical terminology that clients are unfamiliar with will only create confusion or embarrassment and add to the owner's sense of being overwhelmed. When presenting treatment options, it is important to avoid overwhelming the owner with choices and unnecessary detail. First assessing the client's goals and limitations is an integral part of presenting options. When suggesting that the patient's prognosis is poor, keep in mind that only the pet owner can determine the value of the additional time treatment may provide. Clients should be advised that median survival time does not predict what the outcome will be for an individual patient. Balancing realism with optimism is critical for veterinarians treating cancer.

### End-of-Life Decisions

One of the options that veterinary medicine has to offer in order to alleviate pain and suffering is euthanasia. Many cancer cases will conclude with a discussion and an end-of-life decision involving the owner and a member of the healthcare team. Understandably, these discussions can be difficult. Practitioners should be prepared to help the pet owner realize that euthanasia is a humane alternative and a viable option to end a pet's suffering or an unacceptably poor quality of life. Veterinarians should advise clients to consider euthanasia when the clinician can no longer prevent suffering, preserve the pet's quality of life, or otherwise ensure the quality of its death.



## Bo: A Case Study on Canine Osteosarcoma

The case study presented here is an example of how diagnostics and therapeutics can be used in the management of a cancer patient. The case study is not intended to be prescriptive or to imply that the approach taken here is the only way to manage an osteosarcoma patient, nor is it intended to be used as a diagnostic guide. The case history includes the rationale for “decision points,” the interventions the veterinarian would make in appropriately treating the patient.

A 9 yr old neutered male Lab mix named Bo presents with a two-month history of mild lameness in the right front limb. Bo is an outside farm dog from rural Tennessee. He was seen by another veterinarian 1 month ago and placed on a nonsteroidal anti-inflammatory drug for 2 wk. The owners did not see any improvement.

On physical exam, Bo has a body condition score of 4/9. He has a grade 2/4 lameness in the right front limb and is mildly painful over the right carpus with no visible swelling. Distal limb radiographs reveal an osteolytic and proliferative lesion of the distal carpus. The lesion does not cross the joint. Three-view thoracic radiographs reveal no visible lesions and are considered normal.

**Decision point rationale:** Approximately 8% of dogs with osteosarcoma (OSA) have visible metastasis on radiographs at diagnosis. Diseases on the differential list are a metastatic bone tumor and infectious disease (bacterial, fungal). These considerations were discussed with the owner and a fine-needle aspiration (FNA) of the lesion was recommended.

**Decision point rationale:** A FNA often is diagnostic and is less invasive than a bone biopsy. If the cytology is consistent with sarcoma, an alkaline phosphatase (ALP) stain may be used to confirm bony origin.

Cytology of the FNA confirms sarcoma and an ALP stain is positive. Based on these findings, the physical exam, and the patient’s history, a diagnosis of OSA is made.

The patient’s prognosis and treatment options are discussed in detail with the owner. Treatment of the local disease (primary tumor) and systemic disease (micrometastasis) is discussed. Treatment options include surgery (amputation or limb sparing), surgery and chemotherapy, referral for these procedures, referral for definitive radiation therapy, and palliative care. Palliative care includes pain management or referral for palliative radiation.

**Decision point rationale:** If a referral is made, follow-up care by the primary care veterinarian is appropriate. Therefore, it is important that the primary and referral veterinarians discuss postoperative care, follow-up blood work, and management of any potential side effects.

The owner elected to pursue further staging diagnostics

and is considering amputation with follow-up chemotherapy.

A complete blood count, comprehensive chemistry profile, and a urinalysis are performed to rule out comorbidities. Elevated serum ALP is a negative prognostic indicator. Additional staging considerations would entail referral for a bone scan to identify other bone lesions (<10% of cases have detectable bone metastases) and abdominal ultrasound (<10% of dogs have intra-abdominal metastases). Results of Bo’s blood work and urinalysis are normal.

A forelimb amputation is performed with uneventful recovery. At the time of suture removal, carboplatin chemotherapy is initiated and given IV once every 3 wk for a total of four treatments.

**Decision point rationale:** There are multiple chemotherapeutic treatment options for OSA. Chemotherapeutic agents with proven efficacy include doxorubicin, cisplatin, and carboplatin. However, studies generally have not shown clear differences in outcome between the various protocols.

Following surgery Bo returned to normal activity. His quality of life improved after amputation of the forelimb and alleviation of pain. He tolerated his chemotherapy well, but required a few days of anti-emetics after two of the treatments for vomiting.

Three-view thoracic radiographs are performed every three months following completion of chemotherapy. Nine months after the last chemotherapy treatment radiographic evidence of metastasis was found. Bo is normal clinically and enjoying a good quality of life.

The primary care veterinarian discussed Bo’s prognosis with the owner, including the likely terminal nature of the metastatic OSA and scenarios for his quality of life. Because Bo currently has a good quality of life, the owners opted to begin therapy for the metastasis and Bo is placed on a tyrosine kinase inhibitor (TKI) for the management of his metastatic disease.

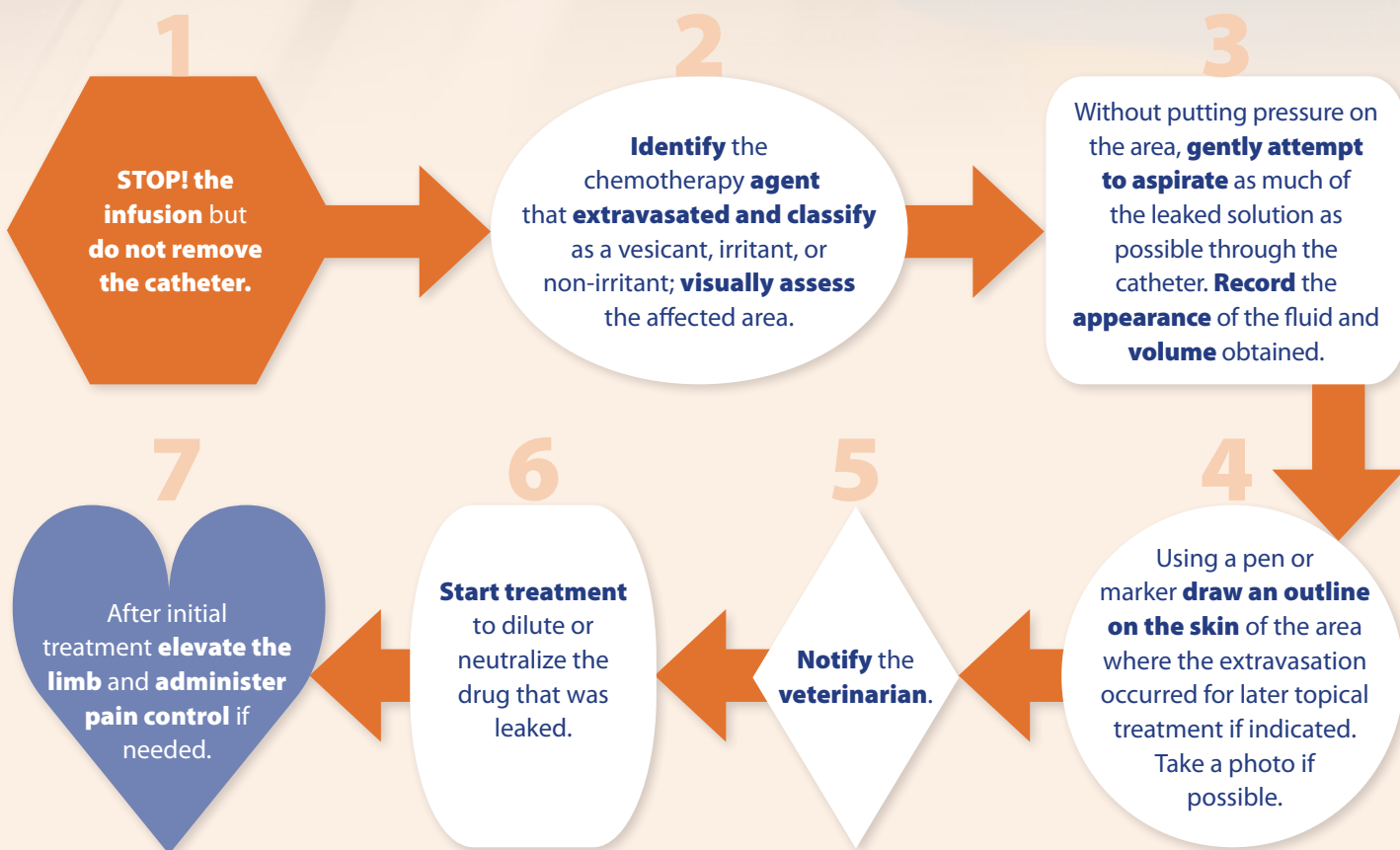
**Decision point rationale:** Cancer should be considered and treated as a chronic disease much like end-stage renal disease or heart failure. Once metastatic disease becomes clinically apparent, a realistic goal of therapy is to attempt to stabilize it or slow its progression. Metronomic chemotherapy and TKIs are both excellent considerations in this scenario. For most owners, maintaining a good quality of life is the most important consideration.

Three months later, three-view thoracic radiographs reveal that Bo’s metastatic disease has not progressed and is stable.

Bo continued to maintain a good quality of life for six months until he eventually became dyspneic. Advanced metastatic disease was documented radiographically, and the owners elected euthanasia at that time.



## 7 Steps for Managing Chemotherapy Extravasation



# Chemotherapy Extravasation Management

Extravasation is a term that describes a drug inadvertently or accidentally leaking into surrounding tissue or the subcutaneous space during IV infusions. The volume, contact time, and drug properties are all factors that have to be considered when assessing an extravasation event. Chemotherapeutic agents are at highest risk for complications due to the nature of the agents and the potential to cause high cellular damage when extravasated. The severity of tissue damage can be limited by quick detection of extravasations and swift treatment. A chemotherapeutic extravasation is considered an oncologic emergency.

When assessing a chemotherapy extravasation, it is important to understand the classification of the chemotherapeutic agent in terms of its potential to cause cellular damage if extravasated. Chemotherapeutics can be classified into three categories: vesicants, irritants, and non-irritants.

Vesicants can cause pain, edema, and erythema, and potentially lead to blisters and tissue necrosis when extravasated. Irritants have been described in human medicine as a burning sensation, pain, and/or erythema during injection and extravasation. Non-irritants do not usually produce local reactions to surrounding tissue; however, mild inflammation has been reported. Among veterinary patients, careful monitoring of the patient and injection site for manifestations of erythema and drug leakage during an injection/infusion would be prudent practice.

Unfortunately at this time, there is not a consensus concerning the management of chemotherapy extravasation in human medicine. Despite a large amount of published literature on this topic, most recommendations are based upon empirical, or anecdotal, evidence. The lack of strength and large variability in management practices in case reports make it difficult to standardize and rank management practice in terms of efficacy. Consequently, this toolkit serves only as a guide for potential treatment options.

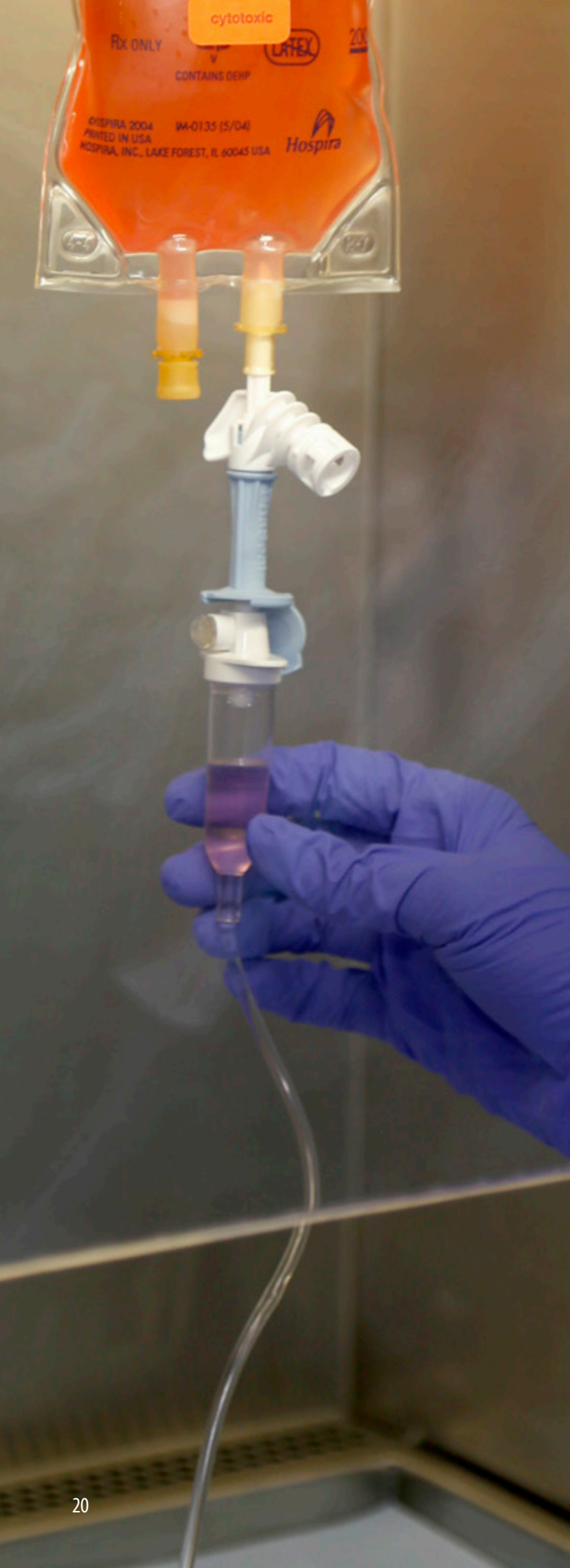
Many chemotherapeutic agents do not have known antidotes that are safe to use in order to neutralize their toxic activity. The algorithm on the opposite page should aid in the decision-making process when handling a chemotherapeutic extravasation. It is important to note that the first goal of treatment is to immediately either localize the extravasated agent or disperse the agent. The choice of localization or dispersion depends on the chemotherapeutic agents. Cold compress will help to constrict local blood vessels and localize tissue damage. Warm compress will act in the opposite, aiding to disperse the chemotherapeutic into surrounding tissues. The second goal of treatment is to neutralize the chemotherapeutic once localized or dilute the agent to allow it to be absorbed and consequently metabolized.

For the purposes of this document, we will focus upon five commonly used chemotherapeutics and their antidotes: doxorubicin, vincristine, vinblastine, carboplatin, and L-asparaginase.

**TABLE 1. MANAGEMENT OF EXTRAVASATION**

<b>Treatment Goal: Localize and Neutralize</b>	<b>Treatment Goal: Disperse and Dilute</b>	<b>Treatment Goal: Monitor for Mild Inflammation</b>																									
<table border="1"> <thead> <tr> <th><i>Vesicants</i></th> <th><i>Irritants</i></th> </tr> </thead> <tbody> <tr> <td>Dactinomycin*</td> <td>Carboplatin*</td> </tr> <tr> <td>Docetaxel*</td> <td>Cisplatin*</td> </tr> <tr> <td>Doxorubicin<sup>†</sup></td> <td>Dacarbazine*</td> </tr> <tr> <td>Mitomycin<sup>‡</sup></td> <td>Fluorouracil*</td> </tr> <tr> <td>Mitoxantrone*</td> <td>Ifosfamide*</td> </tr> <tr> <td>Paclitaxel*</td> <td>Melphalan*</td> </tr> </tbody> </table>	<i>Vesicants</i>	<i>Irritants</i>	Dactinomycin*	Carboplatin*	Docetaxel*	Cisplatin*	Doxorubicin <sup>†</sup>	Dacarbazine*	Mitomycin <sup>‡</sup>	Fluorouracil*	Mitoxantrone*	Ifosfamide*	Paclitaxel*	Melphalan*	<table border="1"> <thead> <tr> <th><i>Vesicants</i></th> </tr> </thead> <tbody> <tr> <td>Vinblastine<sup>§</sup></td> </tr> <tr> <td>Vincristine<sup>§</sup></td> </tr> <tr> <td>Vinorelbine<sup>§</sup></td> </tr> </tbody> </table>	<i>Vesicants</i>	Vinblastine <sup>§</sup>	Vincristine <sup>§</sup>	Vinorelbine <sup>§</sup>	<table border="1"> <thead> <tr> <th><i>Non-Irritants</i></th> </tr> </thead> <tbody> <tr> <td>L-Asparaginase</td> </tr> <tr> <td>Bleomycin</td> </tr> <tr> <td>Cyclophosphamide</td> </tr> <tr> <td>Cytarabine</td> </tr> <tr> <td>Gemcitabine</td> </tr> <tr> <td>Methotrexate</td> </tr> </tbody> </table>	<i>Non-Irritants</i>	L-Asparaginase	Bleomycin	Cyclophosphamide	Cytarabine	Gemcitabine	Methotrexate
<i>Vesicants</i>	<i>Irritants</i>																										
Dactinomycin*	Carboplatin*																										
Docetaxel*	Cisplatin*																										
Doxorubicin <sup>†</sup>	Dacarbazine*																										
Mitomycin <sup>‡</sup>	Fluorouracil*																										
Mitoxantrone*	Ifosfamide*																										
Paclitaxel*	Melphalan*																										
<i>Vesicants</i>																											
Vinblastine <sup>§</sup>																											
Vincristine <sup>§</sup>																											
Vinorelbine <sup>§</sup>																											
<i>Non-Irritants</i>																											
L-Asparaginase																											
Bleomycin																											
Cyclophosphamide																											
Cytarabine																											
Gemcitabine																											
Methotrexate																											
<p><b>1. Localize</b> Apply dry cold compresses for 20–30 min at a time, 4 times a day for the first 24–48 hr following extravasation.</p> <p><b>2. Neutralize</b> Use the antidote specific to the agent.</p>	<p><b>1. Disperse</b> Apply dry warm compresses for 20–30 min at a time, 4 times a day for the first 24–48 hr following extravasation.</p> <p><b>2. Dilute</b> Use the antidote specific to the agent.</p>	<p>Apply dry cold compresses for about 20–30 min, then as needed.</p>																									

\*No recommended antidote. <sup>†</sup>Recommended antidote: dexrazoxane or dimethyl sulfoxide (DMSO). <sup>‡</sup>Recommended antidote: DMSO. <sup>§</sup>Recommended antidote: hyaluronidase. Adapted from [1].



## Anthracycline Extravasations

### Doxorubicin Antidotes

#### Dexrazoxane

Dexrazoxane is an iron chelator that prevents anthracycline-iron complexes and free radical formation causing oxidative damage. Furthermore, dexrazoxane has a protective effect on healthy tissue by stabilizing topoisomerase II, thereby preventing damage from anthracycline. This mechanism of action is responsible for its ability to reduce the cardiotoxicity associated with anthracyclines, such as doxorubicin. Dexrazoxane has the most evidence to support its use in human medicine. In two single arm trials among 54 human patients with anthracycline extravasations, dexrazoxane was shown to be effective in preventing severe tissue damage. Dexrazoxane was administered IV in a three-day schedule (1000, 1000, and 500 mg/m<sup>2</sup> on respective days) starting no later than 6 hr after the extravasation event [2]. In mouse models dexrazoxane has been shown to have protective effects against extravasations 3 hr after extravasations [3].

In veterinary medicine, Venable et al. described four case reports in dogs with doxorubicin extravasation; three dogs received varying doses of dexrazoxane within 2 hr of extravasation and 1 after 48 hr. The dogs that received dexrazoxane within 2 hr made full recoveries with no surgical debridement, whereas the dog that received dexrazoxane 48 hr after the event required surgical debridement. Doses varied from 231 to 500 mg/m<sup>2</sup> with some varying number of doses given [4].

#### Dimethyl sulfoxide (DMSO)

DMSO has been used with success in human anthracycline extravasation. In humans, topical DMSO was applied immediately after extravasation covering twice the area affected. This treatment was repeated twice daily for 14 days with resolution [1]. It is important to note that concomitant use of DMSO and dexrazoxane is not recommended and has been shown, in mice, to decrease dexrazoxane efficacy [5, 6]. However, in a case report of 4 dogs with doxorubicin extravasation, all dogs received dexrazoxane along with topical 90% DMSO ointment every 8 hr for 14 days; only 1 dog required surgical debridement but all survived with medical management [4]. Evidence to support DMSO use for doxorubicin extravasation exists; however, the strength and variability of that data do not support DMSO's use as first-line treatment of doxorubicin extravasation.

## Vinca Alkaloid Extravasations

### Vincristine and Vinblastine Antidotes

#### Hyaluronidase

Hyaluronidase is an enzyme that degrades hyaluronic acid, improving the absorption of the extravasated drugs into circulation where they can be metabolized [1]. A study with seven human patients with accidental vinca alkaloid extravasation showed no skin necrosis after local treatment with hyaluronidase [7]. Data from this study showed use of a 150 U/ml solution of hyaluronidase injected through the existing catheter line was beneficial. The dose was 1:1, 1 ml hyaluronidase (150 U/ml) for every 1 ml of extravasated drug. Warm compresses help disperse vinca alkaloids, which helps minimize vesicant toxicity.

## Alkylating Agents

### Carboplatin

#### DMSO

Application of topical DMSO over the affected skin surface every 8 hr for 1 wk along with a local dry cold compress have been shown to be beneficial in humans [8]. Medical management with antihistamines or anti-inflammatories may be beneficial if needed.

## L-Asparaginase

As **L-asparaginase** is a non-irritant, it is fairly benign. Local dry cold compresses will help with any reactions [1].

### References

1. Fidalgo JA, Pérez L, García Fabregat A, et al. Management of chemotherapy extravasation: ESMO-EONS Clinical Practice Guidelines. *Ann Oncol* 2012; 23 (Supplement 7): vii167–vii173. Oxford University Press. [http://annonc.oxfordjournals.org/content/23/suppl\\_7/vii167.full.pdf](http://annonc.oxfordjournals.org/content/23/suppl_7/vii167.full.pdf). Accessed Mar 3 2015.
2. Mouridsen HT, Langer SW, Buter J, et al. Treatment of anthracycline extravasation with savene (dexrazoxane): results from two prospective clinical multicenter studies. *Ann Oncol* 2007; 18: 546–550.
3. Langer SW, Sehested M, Jensen PB. Treatment of anthracycline extravasation with dexrazoxane. *Clin Cancer Res* 2000; 6: 3680–3686.
4. Venable RO, Saba CF, Endicott MM, et al. Dexrazoxane treatment of doxorubicin extravasation injury in four dogs. *Journal of the American Veterinary Medical Association* 2012; 240(3): 304-07.
5. Langer SW. Extravasation of chemotherapy. *Curr Oncol Rep* 2010; 12(4):242–246. doi: 10.1007/s11912-010-0110-7.
6. Langer SW, Thougard AV, Sehested M, Jensen PB. Treatment of anthracycline extravasation in mice with dexrazoxane with or without DMSO and hydrocortisone. *Cancer Chemother Pharmacol* 2006; 57(1):125–128. doi: 10.1007/s00280-005-0022-7.
7. Bertelli G, Dini D, Forno GB, et al. Hyaluronidase as an antidote to extravasation of vinca alkaloids: clinical results. *J Cancer Res Clin Oncol* 1994; 120: 505–506.
8. Bertelli G, Gozza A, Forno GB, et al. Topical dimethylsulfoxide for the prevention of soft tissue injury After extravasation of vesicant cytotoxic drugs: a prospective clinical study. *J Clin Oncol* 1995; 13: 2851–2855.

### SUMMARY OF CHEMOTHERAPEUTIC ANTIDOTES

Chemotherapy	Classification of Chemotherapy	Antidotes
Doxorubicin	Vesicant	Dexrazoxane—start ASAP, little benefit after 48 hr, or topical 90% DMSO
Vincristine	Vesicant	150 U/ml solution of hyaluronidase injected via the existing catheter
Vinblastine	Vesicant	
Carboplatin	Irritant	Topical 90% DMSO may help, and local dry cold compresses
L-asparaginase	Non-Irritant	None

# AAHA's Resources on Oncology

## 2013 AAHA Referral Guidelines

[aaha.org/referral\\_guidelines](http://aaha.org/referral_guidelines)

Enhance teamwork and bridge the communication gap among general practitioners, specialists, and clients.

## Helping Your Pet Live Life to the Fullest (for clients)

[aaha.org/oncology\\_guidelines](http://aaha.org/oncology_guidelines)

This attractive poster offers basic safety precautions for caretakers of pets undergoing chemotherapy. **Available for accredited practices only.**

## Chemotherapy Extravasation Management

[aaha.org/oncology\\_guidelines](http://aaha.org/oncology_guidelines)

Take quick action when extravasation happens. Use this handout to train staff on general principles and proper procedures for specific chemotherapeutics.

## Personal Protective Equipment Poster

[aaha.org/oncology\\_guidelines](http://aaha.org/oncology_guidelines)

## Living with Cancer Poster

[aaha.org/oncology\\_guidelines](http://aaha.org/oncology_guidelines)

**Additional online version available for accredited practices.**

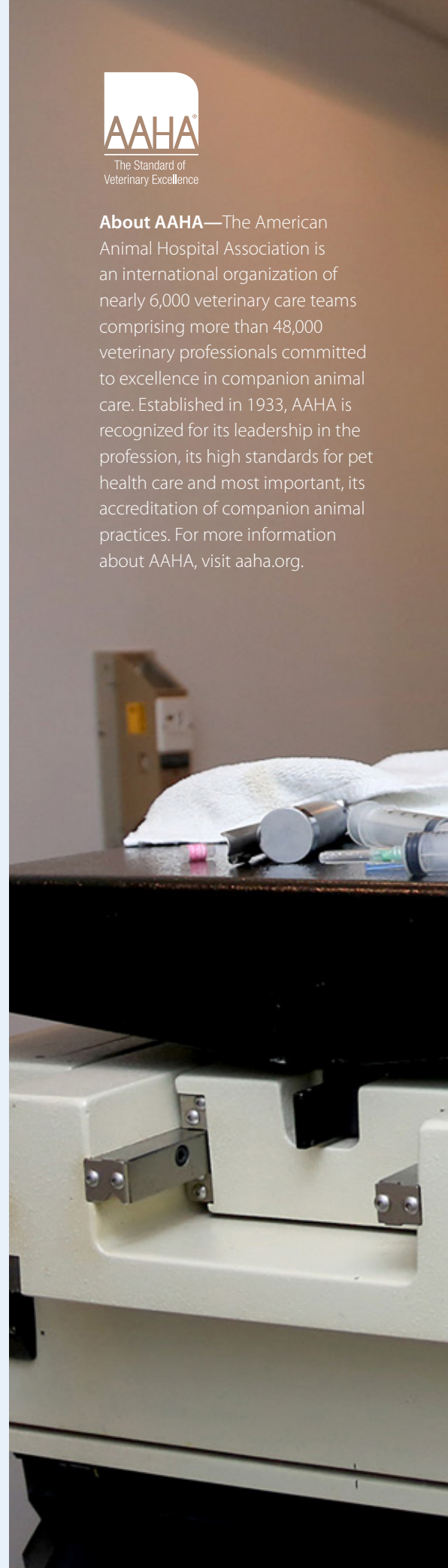


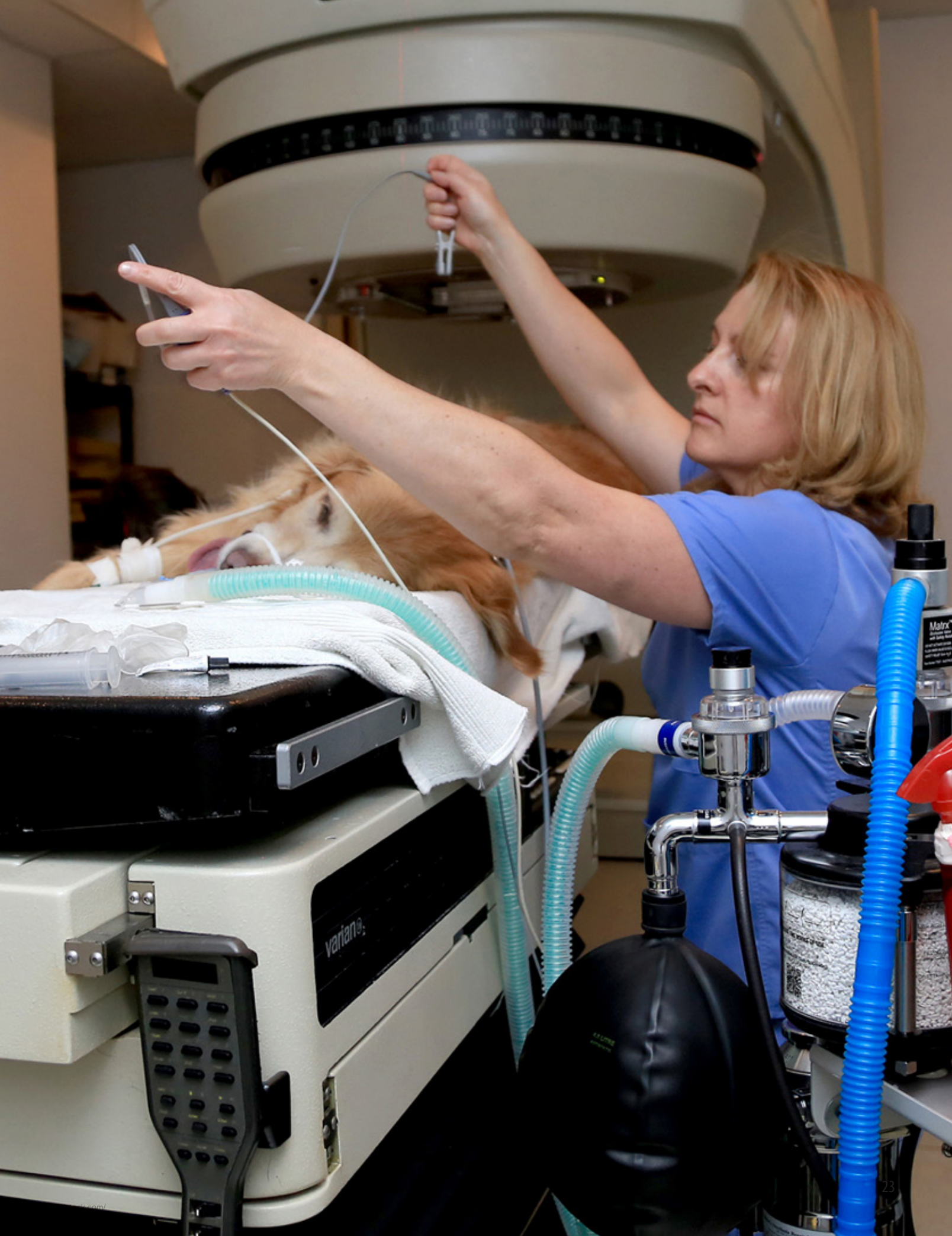
These handouts are available in the AAHA Download Center.

[aaha.org/oncology\\_guidelines](http://aaha.org/oncology_guidelines)



**About AAHA**—The American Animal Hospital Association is an international organization of nearly 6,000 veterinary care teams comprising more than 48,000 veterinary professionals committed to excellence in companion animal care. Established in 1933, AAHA is recognized for its leadership in the profession, its high standards for pet health care and most important, its accreditation of companion animal practices. For more information about AAHA, visit [aaha.org](http://aaha.org).







*Oncology technicians insert Sophie's IV line before preparing her chemotherapy treatment.*

## Living with Cancer

Sophie was diagnosed with a mast cell tumor on her right hock in 2010, when she was nine years old. Following surgery and chemotherapy, Sophie, now a sweet sixteen-year-old, is thriving cancer-free.

Pet owners are beginning to realize what most oncologists have long understood: **a cancer diagnosis is not a death sentence.** More and more pet owners are seeking specialists for cancer treatment, and dogs and cats are living longer, better-quality lives as a result.

This implementation toolkit was developed by the American Animal Hospital Association (AAHA) to provide information for practitioners regarding small animal oncology. The information contained in this toolkit should not be construed as dictating an exclusive protocol, course of treatment, or procedure, nor is it intended to be an AAHA standard of care. This implementation toolkit is sponsored by a generous educational grant from Aratana Therapeutics, Medtronic, and Zoetis.

These guidelines were supported by a generous educational grant from Aratana Therapeutics, Medtronic, and Zoetis.

