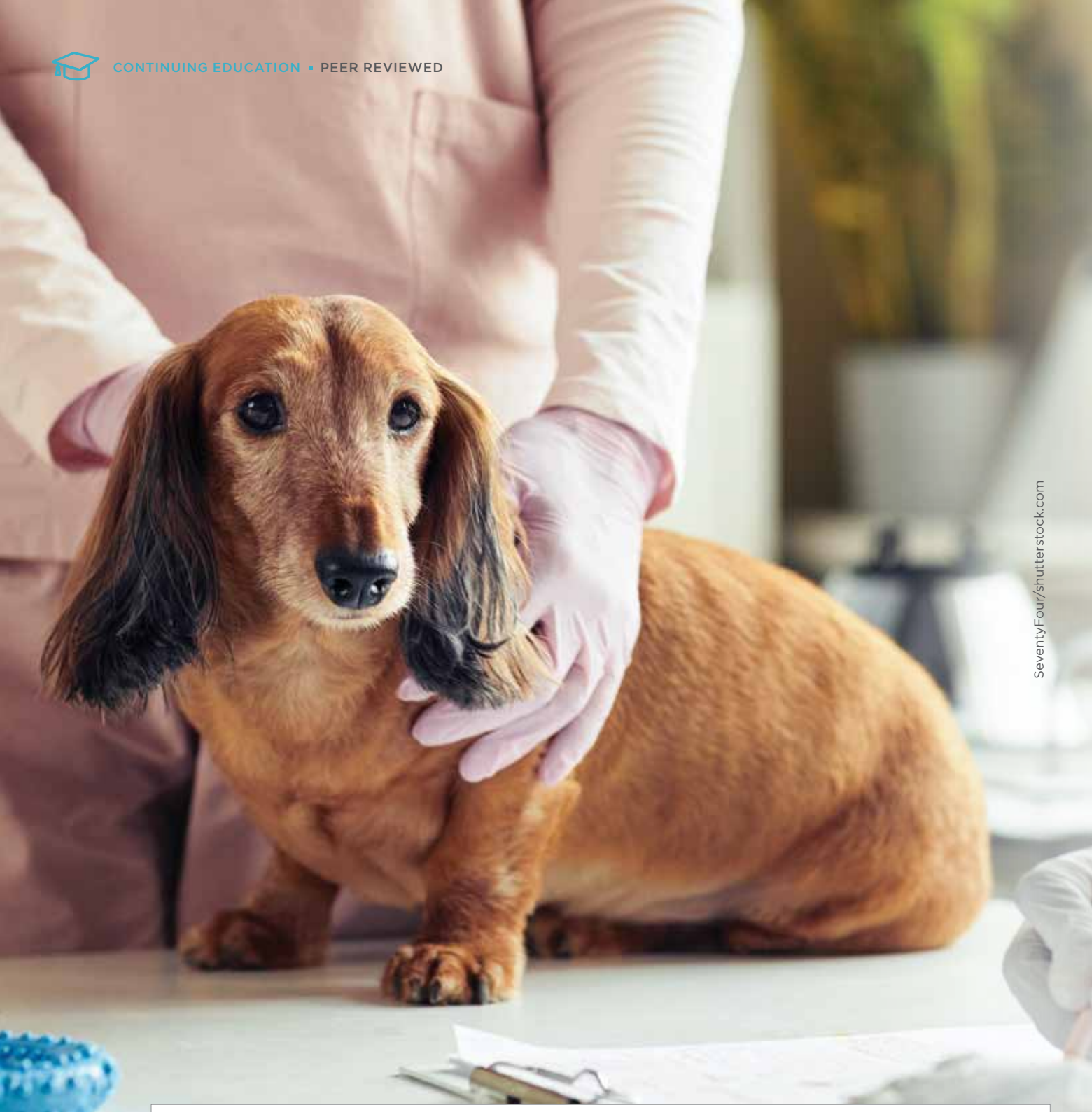

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Abstract

Many companion animals receiving chemotherapy are treated by a board-certified veterinary oncologist. Primary care veterinarians often perform diagnostic tests on these patients' "off" weeks as a part of their treatment protocol. These veterinarians may be asked to dispense antibiotics or supportive care medications to help mitigate adverse effects of cancer treatment. Primary care veterinarians can also monitor patients for recurrence or progression of disease with routine physical examinations and imaging. Thus, the primary care veterinarian plays a crucial role in the care of oncology patients. The monitoring plan for cancer patients depends on the diagnosis, treatment plan, and client's proximity to the veterinary oncology specialist. This article provides an overview of the rationale for recommending interim diagnostics and monitoring for companion animals receiving chemotherapy.

CONTINUING EDUCATION

ONCOLOGY

Monitoring of Chemotherapy Patients in General Practice

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Cancer patients receiving chemotherapy require frequent diagnostic tests to ensure continued response to and tolerance of treatment. Routine follow-up care allows for prompt recognition of disease progression or recurrence when patients complete their treatment protocol. This correlates with better outcomes for many cancer types.[1,2] Most canine and feline patients with hematopoietic diseases in clinical remission experience relapse. Similarly, local or systemic treatments do not cure most patients with high-grade solid tumors. Although they can remain disease-free for some time, progression is anticipated. Therefore, continued care beyond completion of chemotherapy protocols is essential for pets with cancer.

Take-Home Points

- Primary care veterinarians play a crucial role in managing oncology patients, both during treatment and in the post-treatment monitoring period.
- Toxic hematologic effects of chemotherapy are best monitored with serial complete blood counts after treatment, with most drugs causing a neutrophil and platelet nadir 5 to 10 days after administration.
- The risk of infection is likely increased when neutrophil counts fall below 750/µL; however, any patient exhibiting signs of illness during a time of anticipated nadir should be treated for potential sepsis regardless of neutrophil count.
- Obtaining a body temperature (rectal is ideal) at the time of a post-chemotherapy complete blood count is essential for interpreting the patient's potential need for additional therapy in the face of chemotherapy-induced neutropenia.
- Chemotherapy-induced thrombocytopenia is rarely a clinical issue, but severely thrombocytopenic patients (<50 × 10^3/µL) should be monitored for signs of bleeding.
- Gastrointestinal toxicosis secondary to chemotherapy typically occurs 2 to 5 days after treatment and improves within 3 to 5 days of onset. Gastrointestinal supportive care medications (antinausea, antidiarrhea, and appetite stimulant drugs) can help alleviate clinical signs during this period.
- In addition to myelosuppression and gastrointestinal effects, chemotherapy agents can also be associated with organ-specific toxic effects (e.g., hepatotoxicity, cardiotoxicity).
- After treatment, periodic monitoring is recommended for both hematopoietic and solid tumors. Prompt recognition of disease progression generally correlates with better outcomes for many cancers.

BASIC MONITORING TESTS FOR PATIENTS RECEIVING CHEMOTHERAPY

Cytotoxic chemotherapy drugs interfere with cell growth and division.[3] Healthy and neoplastic tissues contain proliferating and resting cells, and both populations are susceptible to damage from chemotherapy drugs. Tissues with higher rates of cell turnover are most vulnerable to injury. This manifests most frequently as clinical signs related to bone marrow suppression (myelosuppression) and adverse gastrointestinal (GI) signs.[3]

Cytotoxic chemotherapy protocols are administered at regular intervals called cycles. Toxic chemotherapeutic effects on sensitive healthy tissues limit the dose and frequency of treatment. Factors including the type and amount of drug can determine the kind and degree of adverse effects. Each patient reacts to chemotherapy in a unique way, with some patients experiencing more severe adverse effects than others.

Complete Blood Count

Myelosuppression results from chemotherapy-induced damage to hematopoietic stem cells (**FIGURE 1**). Therefore, patients undergoing chemotherapy require frequent complete blood counts (CBCs) as part of monitoring. The severity of suppression ranges from mild to severe and is usually temporary but can be permanent with some drugs.

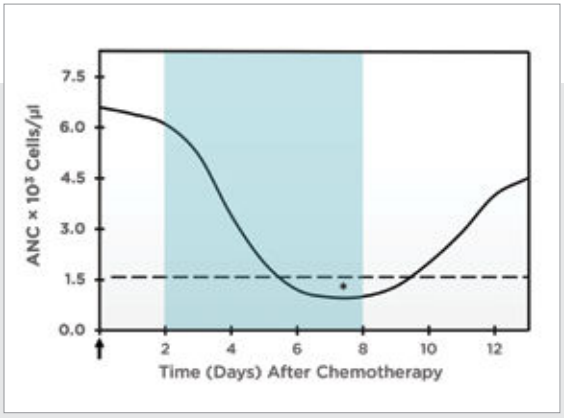


FIGURE 1. Chemotherapy-induced myelosuppression. Chemotherapy is administered on day 0 **(arrow)**. The solid line represents the expected absolute neutrophil count post-treatment for most conventional chemotherapy drugs. The **dashed line** represents the minimal neutrophil count (1500/µL) recommended for subsequent treatment. The **shaded area** represents the predicted time course for gastrointestinal toxicosis after chemotherapy. Patients are at increased risk for bacteremia and sepsis when gastrointestinal toxicosis overlaps with neutropenia **(asterisk)**. ANC = absolute neutrophil count

BOX 1 Checklist for Chemotherapy Outpatient Visits

- History (any signs of gastrointestinal toxicosis, lethargy, or any other owner concerns)
- Body weight
- Physical examination:
  - Mucous membranes/capillary refill time
  - Temperature
  - Heart rate
  - Respiratory rate
  - Blood pressure (if indicated)
- Recommended laboratory tests (e.g., liver enzymes, creatinine, urinalysis)
- Prescribe supportive care medications (e.g., antinausea, antidiarrhea) as needed

Neutrophils have the shortest lifespan in circulation (<24 hours) and are the first cell lines to become depleted following chemotherapy. The neutrophil nadir (lowest count) is anticipated between 5 and 10 days after drug administration. Platelets have the second shortest lifespan (5 to 7 days), and counts may be lowest up to 14 days after treatment. Red blood cells have the most extended lifespan (120 days in dogs, 70 days in cats), and anemia resulting from chemotherapy tends to be mild, chronic, and nonregenerative.

CBCs are performed before chemotherapy treatments to ensure adequate recovery from previous cytopenias. The decision to administer or withhold treatment depends on the absolute neutrophil count (ANC) and platelet count (**FIGURE 2**). Veterinary oncologists use different cutoff values for recommending chemotherapy treatment administration versus delay; the authors use 1500/µL for neutrophils and 50 × 10^3/µL for platelets. Administering chemotherapy in cytopenic patients could delay bone marrow recovery and increase the risk of infection and bleeding. Therefore, if a patient's CBC results are below a cutoff value, chemotherapy is delayed and restarted once the count has reached the minimal cutoff value.

Other Tests

A quick assessment should be performed for all patients presenting for recheck laboratory testing after chemotherapy (**BOX 1**). Body temperature (rectal is ideal) should be measured during a postchemotherapy CBC to interpret the patient's potential need for additional therapy in the face of chemotherapy-induced neutropenia. If the patient is scheduled for additional chemotherapy, see **FIGURE 2**. If receiving lomustine (CCNU [cyclohexylchloroethylnitrosourea]), see

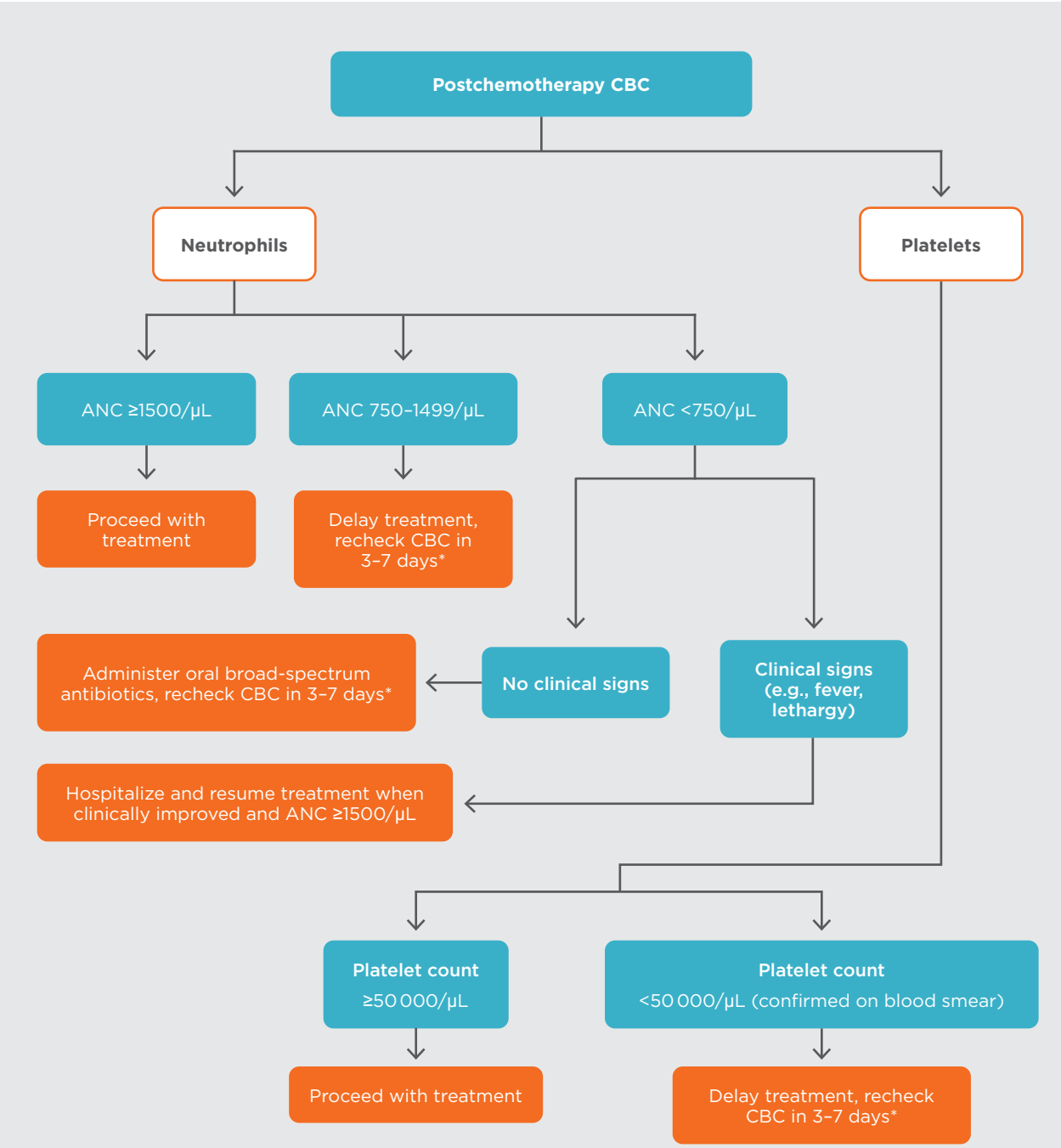


FIGURE 2. Proposed guidelines for treatment decisions based on postchemotherapy complete blood count results. Subsequent chemotherapy can be administered if the absolute neutrophil count and platelet counts are ≥1500/µL and ≥50× 10^3/µL, respectively. CBC = complete blood count; ANC = absolute neutrophil count.

**Treatment should be withheld when cytopenias occur and can resume when counts recover above the minimum cutoff values.*

FIGURE 3. This ensures overall patient health and may aid in recognizing toxic effects of chemotherapy that need urgent medical attention.

TOXIC EFFECTS OF CHEMOTHERAPY

Neutropenia

Neutropenia is the most common cause of chemotherapy delays and dose reductions.[3] The ANC, not the percent neutrophils or total leukocyte count, is used to determine the nadir. It is standard practice to recheck a CBC 7 days after chemotherapy administration to detect the anticipated nadir, although the actual nadir may occur earlier or later. Some drugs (e.g., carboplatin) are expected to have a delayed or prolonged nadir; for these, a CBC is checked 14 days post-treatment as well. The value and timing of the neutrophil nadir after the first dose of a chemotherapy drug usually predict response to subsequent doses of the same drug. The ideal neutrophil nadir post-

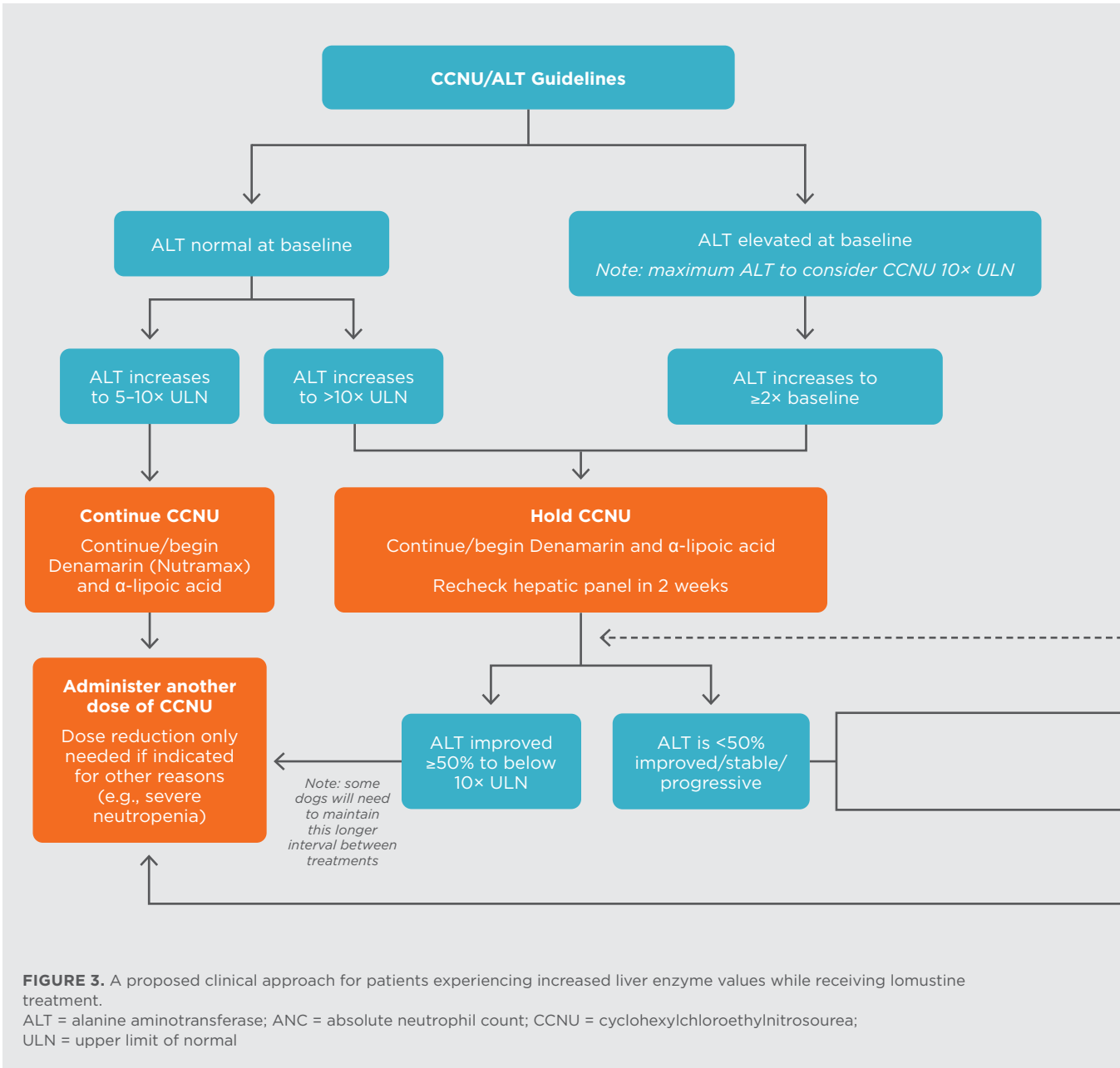
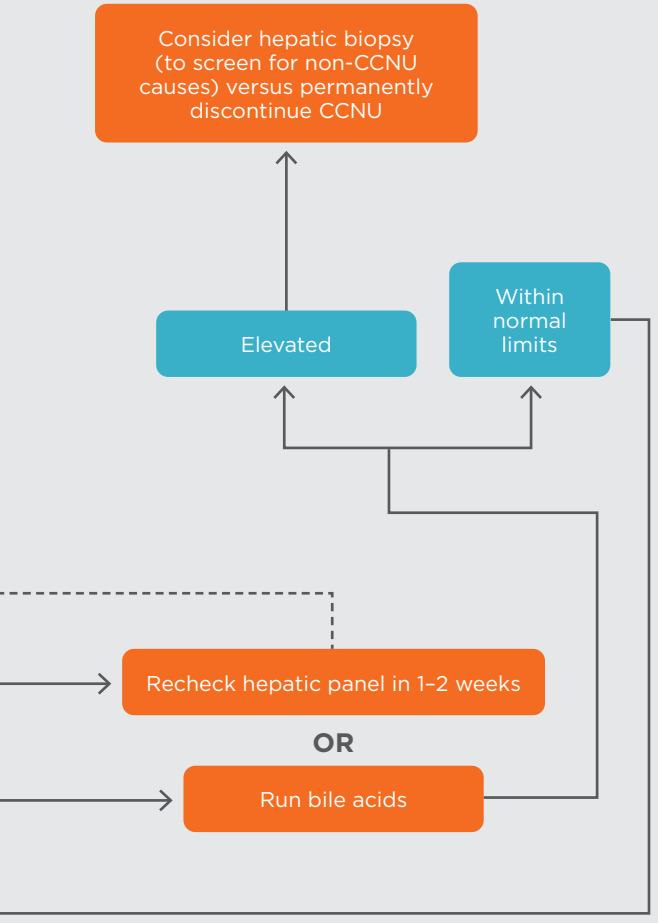


FIGURE 3. A proposed clinical approach for patients experiencing increased liver enzyme values while receiving lomustine treatment.
ALT = alanine aminotransferase; ANC = absolute neutrophil count; CCNU = cyclohexylchloroethylnitrosourea; ULN = upper limit of normal

treatment is ~1000/µL, a value that is unlikely to put the patient at risk for infection but indicates the systemic activity of the drug.[4] Asymptomatic and afebrile neutropenic patients are treated on an outpatient basis. The authors' cutoff value to prescribe oral broad-spectrum antibiotics is an ANC ≤750/µL. If the ANC falls below the cutoff value, a CBC can be rechecked 3 to 7 days later, which is the time it takes for the bone marrow stem cells to recover the neutrophil cell line. Treatment can be resumed once the ANC recovers above the minimum cutoff value.



Neutropenic patients are at risk for infection, specifically bacterial infection, secondary to translocation of the normal commensal flora from their own GI tract or skin.[5] To avoid nosocomial infection, hospitalization of asymptomatic neutropenic patients is not recommended. Dogs with febrile neutropenia can show signs such as lethargy, dehydration, anorexia, vomiting, and diarrhea. Treatment of febrile neutropenic patients includes immediate hospitalization with antibiotic therapy for gram-positive and gram-negative bacteria. The authors empirically use ampicillin-sulbactam (30 mg/kg IV q8h) and enrofloxacin (10 mg/kg IV q24h). Most patients respond rapidly to therapy, although this is a potentially life-threatening condition. Patients are discharged when their temperature has been normal for ~24 hours.

Any patient exhibiting signs of illness during their anticipated nadir should be treated for potential sepsis regardless of neutrophil count.

Thrombocytopenia

Chemotherapy-induced thrombocytopenia is common but is rarely a clinical problem. Most thrombocytopenic patients remain healthy and can be monitored by their owners. They should have moderate activity restrictions, be permitted to go on short leash walks, and avoid chewing on hard toys and bones.

Patients with severe thrombocytopenia ($<50 \times 10^3/\mu L$) can be at risk for spontaneous bleeding. This can manifest as bruising of the skin/petechiae, nosebleeds, bleeding gums, and blood in the urine and stool. In the event of severe bleeding, patients should be promptly assessed. Blood products (e.g., packed red blood cells, platelet-rich plasma) and GI protectants (omeprazole and sucralfate) are used in patients with acute blood loss. A CBC can be rechecked 3 to 7 days following concern for a platelet nadir to document an improvement or recovery of the platelet count.

Gastrointestinal Toxicity

The most rapidly proliferating compartment of the GI tract is the cells lining the crypts. In healthy animals, epithelial cells along the villi are replaced by the crypt cells from below. When crypt cells are damaged from chemotherapy, no replacement cells are available. This results in delayed GI toxicosis manifesting as nausea, hyporexia, vomiting, and diarrhea 2 to 5 days post-treatment. These changes also create a favorable

TABLE 1 Commonly Used Supportive Care Medications in Patients Experiencing Toxic Effects of Chemotherapy

TOXIC EFFECT	SUPPORTIVE CARE MEDICATIONS
Nausea/vomiting	▪ Antinausea drugs ▪ Maropitant 2 mg/kg PO q24h (1 mg/kg for cats) ▪ Ondansetron 0.5–1 mg/kg PO q8–12h ▪ Metoclopramide (if not actively experiencing diarrhea) 0.5 mg/kg PO q8–12h
Hyporexia/anorexia	▪ Appetite stimulants (should only be used in patients with no clinical signs of nausea) ▪ Capromorelin 3 mg/kg PO q24h ▪ Mirtazapine (varying dose ranges in dogs and cats) ▪ Prednisone or prednisolone 1–2 mg/kg PO q24h
Soft stool/diarrhea	▪ Bland/high-fiber diets ▪ Antidiarrheals ▪ Crofelemer delayed-release tablets (125 mg q12h for 3 days for dogs up to 140 pounds [63.5 kg]) ▪ Metronidazole (10 mg/kg PO q12h) or tylosin (10–15 mg/kg PO q12h) ▪ Loperamide 0.1–0.2 mg/kg PO q8–12h ▪ Hydrated calcium aluminosilicate (e.g., Rx Clay; Rx Vitamins, rxvitamins.com)
Elevated alanine aminotransferase	▪ S-Adenosylmethionine and silybin products (Denamarin [Nutramax, denamarin.com] dosed per weight range and given on an empty stomach) ▪ α-lipoic acid 5–10 mg/kg PO q12h

environment for bacterial overgrowth and translocation, which increases the risk of bacteremia and sepsis in neutropenic patients (**FIGURE 2**).[5]

GI toxicosis is usually mild and self-limiting but can be moderate to severe, particularly with certain drugs (e.g., doxorubicin). Moderate to severe GI toxicosis can cause delay or dose reductions for subsequent treatment, diminish the patient's quality of life, and perhaps become a financial burden for the client (e.g., hospitalization). This could lead to discontinuation of treatment.

A complete recovery is typical within 3 to 5 days with healing of the GI mucosa and appropriate supportive care (**TABLE 1**). Treatment of toxic GI effects is symptomatic and consists of bland diets and antiemetic/antinausea drugs such as maropitant and ondansetron. Antidiarrheals are prescribed as needed. The U.S. Food and Drug Administration–approved oral tablet Canalevia-CA1 (crofelemer delayed-release tablets; Jaguar Animal Health, canalevia.com) or antibiotics such as metronidazole and tylosin are commonly used. Loperamide, many natural products such as hydrated calcium aluminosilicate (e.g., Rx Clay; Rx Vitamins, rxvitamins.com), probiotics, and high-fiber foods can be helpful. It is important to monitor body weight and caloric intake in patients experiencing adverse GI signs from chemotherapy. Although there is much debate surrounding feeding tubes in cancer patients, they can be appropriate as a temporary measure to support anorectic patients.

Treatment of toxic GI effects is symptomatic and consists of bland diets and antiemetic/antinausea drugs such as maropitant and ondansetron.

Some chemotherapy drugs cause direct stimulation of the chemoreceptor trigger zone, resulting in acute nausea and vomiting within 24 hours of administration. This effect is common with specific chemotherapy drugs such as cisplatin, dacarbazine, and streptozotocin.[3] Administration of antiemetics before and after such medications reduces the risk of acute nausea and vomiting.

Vincristine can cause paralytic ileus in dogs and cats, beginning ~10 days post-treatment. Signs include abdominal distention, nausea, drooling, vomiting, and anorexia. Treatment is symptomatic. Metoclopramide can help improve clinical signs. The authors substitute vinblastine for vincristine in affected dogs and cats.

Dose reductions (or, in some cases, elimination or substitution) of drugs is warranted any time a patient develops significant clinical signs from a treatment. This includes patients requiring hospitalization or

Case Example: Monitoring Chemotherapy in a Labrador Retriever

Bailey, a 7-year-old female spayed Labrador retriever, was diagnosed with high-grade lymphoma and referred to a medical oncologist. Baseline complete blood count (CBC) and chemistry revealed mild nonregenerative anemia (hematocrit [HCT] 34.6%; reference range, 40.2%–61.2%) and was otherwise unremarkable. Imaging was not performed.

Treatment

Bailey was started on chemotherapy consisting of injectable vincristine, oral cyclophosphamide, injectable doxorubicin, and oral prednisone (CHOP protocol; TABLE A). Bailey received her first dose of vincristine in the hospital and was sent home with cyclophosphamide and furosemide with instructions to have her primary care veterinarian perform a CBC 1 week later before the administration of these drugs at home.

On presentation to her primary care veterinarian on day 7, Bailey's vitals were within normal limits and her lymph nodes were reduced in size. A recheck CBC showed a static nonregenerative anemia (HCT 34.2%), mild neutropenia with an absolute neutrophil count (ANC) of 2100/µL (reference range, 2840–9110/µL), and a normal platelet count. Results of the CBC and vitals were relayed to Bailey's oncologist via email. Based on adequate neutrophil and platelet counts, absence of overt adverse gastrointestinal or other signs, and normal vitals, Bailey's owners were instructed to administer chemotherapy as planned.

One week later, Bailey was presented to her oncologist to receive doxorubicin. On examination, her vitals were within normal limits and her lymph nodes were small and smooth, consistent with clinical remission. Her CBC showed a static nonregenerative anemia (HCT 34.4%), neutropenia with an ANC of 600/µL, and thrombocytopenia at 86 × 10^3/µL (reference range, 290 × 10^3/µL–468 × 10^3/µL). Her ANC was below the cutoff of 1500/µL, so chemotherapy was postponed. The ANC also fell below the threshold for concern for infection, so she was prescribed marbofloxacin (3–5 mg/kg PO q24h for 7 days). A recheck CBC 5 days later revealed complete recovery of her neutrophil and platelet counts to within the reference ranges, and she was administered doxorubicin.

Monitoring

Seven days after doxorubicin administration, Bailey's owners were instructed to recheck a CBC at her primary care veterinarian's office. While Bailey was not due for treatment, the CBC was done to monitor her counts following treatment with a new drug. At that time, her owner reported Bailey was lethargic and hyporexic. On examination, she was 6% to 8% dehydrated and her rectal temperature was 40.4 °C (104.8 °F). Blood analysis revealed an ANC of 470/µL and thrombocytopenia of 110 × 10^3/µL. After communication with Bailey's oncology team, Bailey was admitted for IV fluid therapy. Antinausea medications and IV broad-spectrum antibiotics were also initiated.

The following day, Bailey's temperature, demeanor, and appetite improved. A CBC was rechecked 48 hours later and revealed an ANC of 1700/µL. Because Bailey was afebrile and her appetite was normal, she was discharged and continued on oral broad-spectrum antibiotics. A CBC was rechecked 5 days later and Bailey's cell counts were within normal limits. Bailey was administered vincristine as planned.

Discussion

This case example demonstrates the importance of rechecking a CBC before administering chemotherapy. Bailey's doxorubicin was delayed owing to neutropenia from cyclophosphamide. Despite being severely neutropenic following cyclophosphamide, Bailey continued to do well at home with oral antibiotics. Once her cell counts recovered, she was treated with a standard dose of doxorubicin but experienced more severe hematologic and gastrointestinal effects with this drug. To avoid overt toxicosis and maintain quality of life, Bailey's subsequent dose of cyclophosphamide and doxorubicin should be reduced. A CBC should be rechecked 1 week after the dose reduction to ensure the reduction eliminated the risk of her subsequently developing episodes of febrile neutropenia.

TABLE A CHOP Protocol for Canine Lymphoma[a]

Week 1	Injectable vincristine
Week 2	Oral cyclophosphamide
Week 3	Doxorubicin
Week 4	Off week; cycle is repeated ×4

[a]CHOP protocol used by the authors; drugs are given 7 days apart. The 4 weeks depicted in this table are equal to 1 cycle of CHOP. The cycle is repeated 4 times, as long as the patient tolerates and responds to the drugs; the protocol duration is 16 weeks.

Doxorubicin can cause cumulative cardiotoxic effects in dogs.[9] Ideally, patients undergo a pretreatment cardiac evaluation, including electrocardiography (ECG) and echocardiography.

extensive at-home supportive care or owner requests for modification. Dose reductions are also warranted for patients with numerically significant neutropenia (<1000/µL) and/or thrombocytopenia (<50× 10^3/µL), regardless of clinical signs. The authors typically begin with a 10% reduction in dosage. The **CASE EXAMPLE** sidebar describes dose reduction based on neutropenia.

Hepatotoxicity

CCNU is associated with liver injury in dogs. The injury occurs with cumulative doses. Increased alanine aminotransferase (ALT) is a marker of liver damage from CCNU toxicity.[6] Baseline liver enzyme activities, including ALT and alkaline phosphatase, are assessed before and regularly monitored during treatment. Drug administration can be delayed or discontinued depending on the magnitude of ALT elevation. Guidelines for approaching patients experiencing increased liver enzyme values while receiving CCNU are presented in **FIGURE 2**. Hepatoprotectants such as S-adenosylmethionine and silybin products (e.g., Denamarin; Nutramax, denamarin.com) and α-lipoic acid are recommended at the start of treatment (**TABLE 1**).[7]

Nephrotoxicity

Doxorubicin is associated with irreversible cumulative kidney toxicosis in cats.[8] Measurement of renal parameters (creatinine and blood urea nitrogen) and urine specific gravity is recommended before each doxorubicin treatment. Doxorubicin is not recommended in cats with moderate to severe kidney disease and is discontinued in cats with progressive azotemia.

Cardiotoxicity

Doxorubicin can cause cumulative cardiotoxic effects in dogs.[9] Ideally, patients undergo a pretreatment cardiac evaluation, including electrocardiography (ECG) and echocardiography. Any arrhythmia or murmur newly noted during doxorubicin treatment prompts further evaluation with echocardiography and ECG. Doxorubicin is typically discontinued in patients with cardiotoxic effects.

Sterile Hemorrhagic Cystitis

Sterile hemorrhagic cystitis (SHC) is defined as diffuse inflammation of the urinary bladder wall without an infectious etiology. It is a complication of the alkylating agents cyclophosphamide and ifosfamide.[3] Clinical signs develop within a few days after treatment, including hematuria, dysuria, and pollakiuria. Administration of the causative drug is discontinued. Treatment is aimed at decreasing discomfort associated with cystitis with a nonsteroidal anti-inflammatory drug (NSAID) if clinically safe for the patient. Most cases resolve with time, but SHC can take several weeks to months to subside. Signs are rarely permanent.

MONITORING PATIENTS RECEIVING METRONOMIC CHEMOTHERAPY

Metronomic chemotherapy is the chronic administration of low doses of oral chemotherapy (e.g., daily or every other day). Chlorambucil or cyclophosphamide is commonly administered in this setting in conjunction with an NSAID. Due to the lower dose and reduced risks of toxicosis, monitoring is less intensive and less frequent than conventional chemotherapy. The authors monitor CBCs monthly for the first 3 months. If treatment is well tolerated, CBCs are spaced out to every other month in conjunction with periodic serum biochemical profiles.

Palladia (toceranib phosphate; Zoetis, zoetisus.com) is an oral chemotherapy drug used in the metronomic setting for various cancers. In addition to myelosuppression and GI upset, Palladia is associated with hepatopathy, hypertension, and proteinuria. Laboratory tests, including a CBC, serum biochemical profile, urinalysis (including urine protein:creatinine ratio if there is evidence of proteinuria), and blood pressure, are monitored monthly for 3 to 6 months. If well tolerated, rechecks can be spaced out to every 2 months for as long as the patient receives treatment.

MONITORING PROGRESSIVE DISEASE AND RECURRENCE

Hematopoietic Cancers

Patients with hematopoietic cancers are rarely cured with chemotherapy alone, and most eventually relapse after completing their chemotherapy protocol. Monthly physical examinations and imaging are recommended during the monitoring phase for patients with high-grade diseases (e.g., lymphoma, acute leukemia). Any previously enlarged peripheral lymph nodes are palpated and measured with calipers. CBC with pathologist review is an additional monitoring tool to track cell counts in leukemic patients. Patients with low-grade diseases (e.g., indolent lymphoma, chronic leukemia) are monitored every 2 to 3 months with physical examinations, CBCs, and imaging (if indicated).

Solid Tumors

Surgery is the primary treatment for most non-metastatic solid tumors. The risks of local recurrence depend on factors including tumor type, grade, and histopathologic margins. Periodic physical examinations (e.g., every 2 to 3 months for the first year after surgery, every 6 months thereafter) allow for prompt recognition of local recurrence. Early detection and additional treatment of localized tumors increase the likelihood of treatment success. Enlarged and/or firm lymph nodes should be sampled via fine-needle aspiration (with or without biopsy) to look for evidence of metastasis. Any new cutaneous/subcutaneous masses should also be examined. In tumors with higher risks of distant metastasis, thoracic and abdominal imaging every 2 to 3 months can be considered to look for evidence of metastasis or disease progression.

SUMMARY

Successful treatment of pets with chemotherapy requires knowledge of the effects of the drugs, including anticipated consequences and the expected timing of these events. Veterinary oncologists frequently recommend diagnostic testing in the interim period between treatments for specific purposes, such as monitoring for anticipated hematologic nadirs, potential development of end-organ toxicoses, or evaluation of a patient's remission status. The patient's primary care veterinarian plays a crucial role in routine monitoring during and after treatment. TVP

References

1. Milovancev M, Tuohy JL, Townsend KL, Irvin VL. Influence of surgical margin completeness on the risk of local tumour recurrence in canine cutaneous and subcutaneous soft tissue sarcoma: a systematic review and meta-analysis. *Vet Comp Oncol*. 2019;17(3):354-364. doi:10.1111/vco.12479
2. Horta RS, Lavalle GE, Monteiro LN, Souza MCC, Cassali GD, Araújo RB. Assessment of canine mast cell tumor mortality risk based on clinical, histologic, immunohistochemical, and molecular features. *Vet Pathol*. 2018;55(2):212-223. doi:10.1177/0300985817747325
3. Gustafson DL, Bailey DB. Cancer chemotherapy. In: Vail DM, Thamm DH, Liptak JM, eds. *Withrow & MacEwen's Small Animal Clinical Oncology*. 6th ed. WB Saunders; 2019:182-208.
4. Fournier Q, Serra JC, Handel I, Lawrence J. Impact of pretreatment neutrophil count on chemotherapy administration and toxicity in dogs with lymphoma treated with CHOP chemotherapy. *J Vet Intern Med*. 2018;32(1):384-393. doi:10.1111/jvim.14895
5. Bisson JL, Argyle DJ, Argyle SA. Antibiotic prophylaxis in veterinary cancer chemotherapy: a review and recommendations. *Vet Comp Oncol*. 2018;16(3):301-310. doi:10.1111/vco.12406
6. Kristal O, Rassnick KM, Gliatto JM, et al. Hepatotoxicity associated with CCNU (lomustine) chemotherapy in dogs. *J Vet Intern Med*. 2004;18(1):75-80. doi:10.1892/0891-6640(2004)18<75:hawclc>2.0.co;2
7. Skorupski KA, Hammond GM, Irish AM, et al. Prospective randomized clinical trial assessing the efficacy of Denamarin for prevention of CCNU-induced hepatopathy in tumor-bearing dogs. *J Vet Intern Med*. 2011;25(4):838-845. doi:10.1111/j.1939-1676.2011.0743.x
8. O'Keefe DA, Sisson DD, Gelberg HB, Schaeffer DJ, Krawiec DR. Systemic toxicity associated with doxorubicin administration in cats. *J Vet Intern Med*. 1993;7(5):309-317. doi:10.1111/j.1939-1676.1993.tb01024.x
9. Billingham ME, Mason JW, Bristow MR, Daniels JR. Anthracycline cardiomyopathy monitored by morphologic changes. *Cancer Treat Rep*. 1978;62(6):865-872.

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CONTINUING EDUCATION

Monitoring of Chemotherapy Patients in General Practice

TOPIC OVERVIEW

Many companion animals receiving chemotherapy are treated by a board-certified oncologist. Primary care veterinarians often perform diagnostic tests on these patients' "off" weeks as part of their treatment protocol. These veterinarians may be asked to dispense antibiotics or supportive care medications to help mitigate adverse effects of cancer treatment. Primary care veterinarians can also monitor patients for recurrence or progression of disease with routine physical examinations and imaging. Thus, the primary care veterinarian plays a crucial role in the care of oncology patients. The monitoring plan for cancer patients depends on the diagnosis, treatment plan, and client's proximity to the veterinary oncology specialist. This article provides an overview of the rationale for recommending interim diagnostics and monitoring for companion animals receiving chemotherapy.

LEARNING OBJECTIVES

After reading this article, the reader should be able to describe the rationale for recommended diagnostic tests for oncology patients during and after treatment as well as recognize anticipated complications from treatments, including timing of onset, duration, presenting signs, and what constitutes the need for emergent treatment.

This article has been submitted for **RACE approval for 1 hour of continuing education credit** and will be opened for enrollment upon approval. To receive credit, take the test at **vetfolio.com** by searching the name of the article or scanning the QR code below. 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. **For most chemotherapy drugs, the timing of neutrophil and platelet nadirs is between _____ days.**
   a. 1 and 5
   b. 5 and 10
   c. 10 and 14
   d. 16 and 21

2. **The purpose of performing a complete blood count (CBC) at the time of the anticipated neutrophil nadir after administration of cytotoxic drugs is to:**
   a. Assess the risk for sepsis and the need for prophylactic antibiotics
   b. Determine whether the dosage of the chemotherapeutic drug needs to be adjusted
   c. Ensure the neutrophil count is above the minimum cutoff value to administer subsequent chemotherapy
   d. All of the above

3. **Which chemotherapy drug can cause hepatotoxicity in dogs?**
   a. Lomustine/CCNU
   b. Doxorubicin
   c. Vincristine
   d. Cyclophosphamide

Questions 4 and 5 pertain to the following case:

Marlin, an 8-year-old male neutered Labrador retriever, was started on the CHOP chemotherapy protocol for high-grade lymphoma. Marlin presented to his primary care veterinarian 1 week after receiving his first dose of doxorubicin. The owners reported that Marlin had been hyporexic and his stools had been loose for the past couple of days. On presentation, he was lethargic. His rectal temperature was 40.2 °C (104.5 °F). He was in clinical remission. His CBC showed neutropenia (250/µL) and thrombocytopenia (88 000/µL).

4. **Which of the following statements best applies to Marlin's case?**
   a. Treatment with oral broad-spectrum antibiotics on an outpatient basis will overcome the risk of infection.
   b. The risk of nosocomial infection outweighs the benefit of hospitalization for supportive care.
   c. Gastrointestinal protectants, including omeprazole and sucralfate, are necessary to minimize bleeding risks.
   d. Fever indicates systemic infection, a potentially life-threatening complication justifying hospitalization.

5. **Which strategy minimizes the chance of Marlin experiencing neutropenia following subsequent doxorubicin treatments?**
   a. Reduce his doxorubicin dose by at least 10%.
   b. Marlin cannot safely receive doxorubicin; a different chemotherapy drug effective against lymphoma should be substituted.
   c. Administer the same dose of doxorubicin and prescribe prophylactic antibiotics.
   d. Increase the interval between Marlin's future chemotherapy treatments.

6. **A 5-year-old male neutered Great Dane with osteosarcoma is treated with carboplatin chemotherapy every 3 weeks. He tolerated his first treatment with no complications and is presented for his second dose. His CBC shows neutropenia of 1180/µL. What is the appropriate next step?**
   a. Delay treatment because the neutrophil count is below the cutoff value for treatment.
   b. Delay treatment because of the risk for neutropenic sepsis.
   c. Administer treatment with a 20% dose reduction to avoid causing further neutropenia.
   d. Administer treatment at the previous dose with prophylactic antibiotics.

7. **Which toxic effect is associated with doxorubicin in dogs?**
   a. Ototoxicity
   b. Hepatotoxicity
   c. Cardiotoxicity
   d. Neurotoxicity

8. **Which laboratory parameter(s) must be monitored in cats treated with doxorubicin?**
   a. Creatinine and blood urea nitrogen serum concentration
   b. Alanine aminotransferase serum concentration
   c. NT-proBNP plasma concentration
   d. B_{12} and folate serum concentration

9. **Gastrointestinal toxicosis from chemotherapy most commonly occurs within what time frame after treatment?**
   a. Immediately after treatment
   b. 1 to 2 days
   c. 2 to 5 days
   d. 7 to 10 days

10. **Which of the following statements regarding sepsis in the context of neutropenic chemotherapy patients is false?**
    a. Sepsis is always accompanied by fever in neutropenic animals.
    b. The risk for sepsis is reduced with careful monitoring and appropriate prophylactic antibiotic therapy.
    c. When sepsis progresses to septic shock, the prognosis is poor.
    d. The risk of sepsis after chemotherapy is likely increased when neutrophil counts are below 750/µL.