October 2018

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FLUID THERAPY OVERVIEW

IN THIS ISSUE

Volume 16 Number 10

WSAVA Global Veterinary Community

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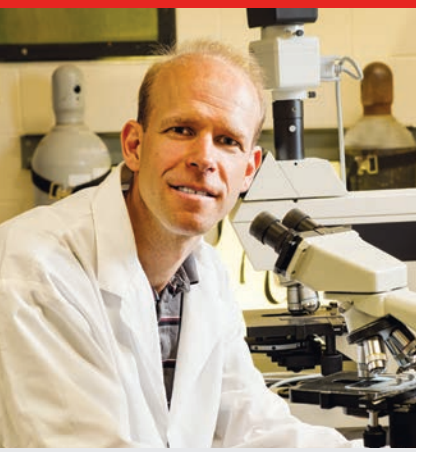

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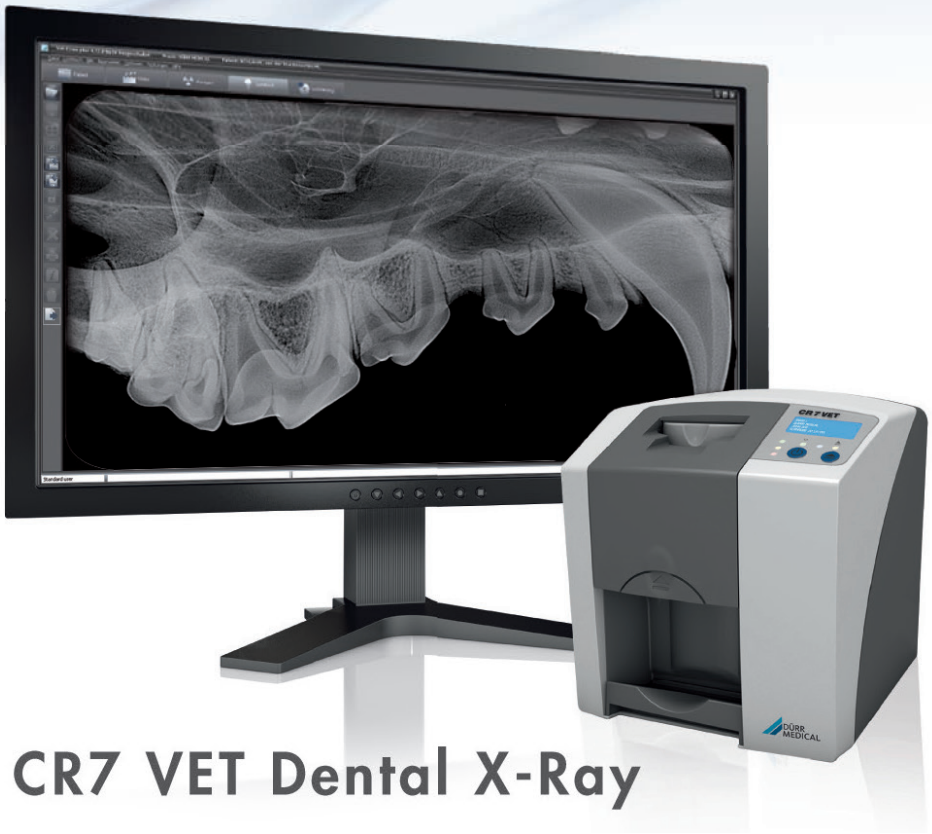

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Clinician's Brief (ISSN 1542-4014) is published monthly by Brief Media, an Educational Concepts company, 2021 S Lewis Avenue, #760, Tulsa, OK 74104.

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Domestic subscription rate: $65.00 per year. Single copy: $8.00. Payments by check must be in US funds on a US branch of a US bank only; credit cards also accepted.

POSTMASTER: Send address changes to Brief Media, PO Box 1084, Skokie, IL 1084 60076-9969. Canada Post publications mail agreement #40932038: Return undeliverable Canadian mailings to Circulation Dept; 7496 Bath Rd, Unit #2; Mississauga, ON L4T 1L2. Periodicals postage paid at Tulsa, OK, and at additional mailing offices.

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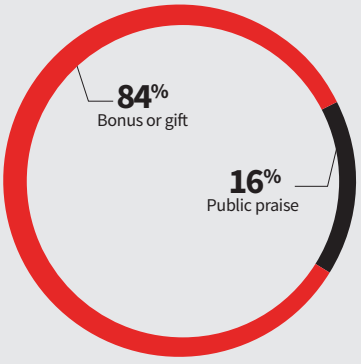

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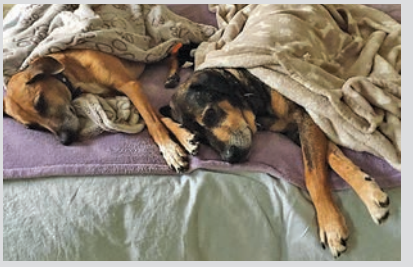

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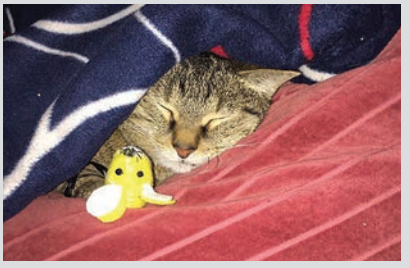

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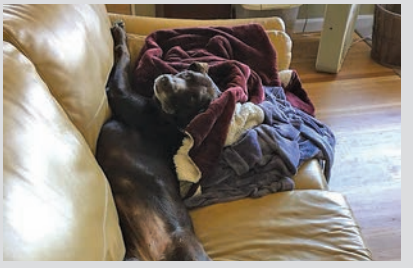

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[1]Hill's® Prescription Diet® k/d® feline with chicken dry food. [2]Data on file. Hill's Pet Nutrition, Inc. 2018. Results are average values with statistical significance (p value less than or equal to 0.05). [3]Royal Canin™ Veterinary Diet Renal Support A Feline, dry food sold in the US market.

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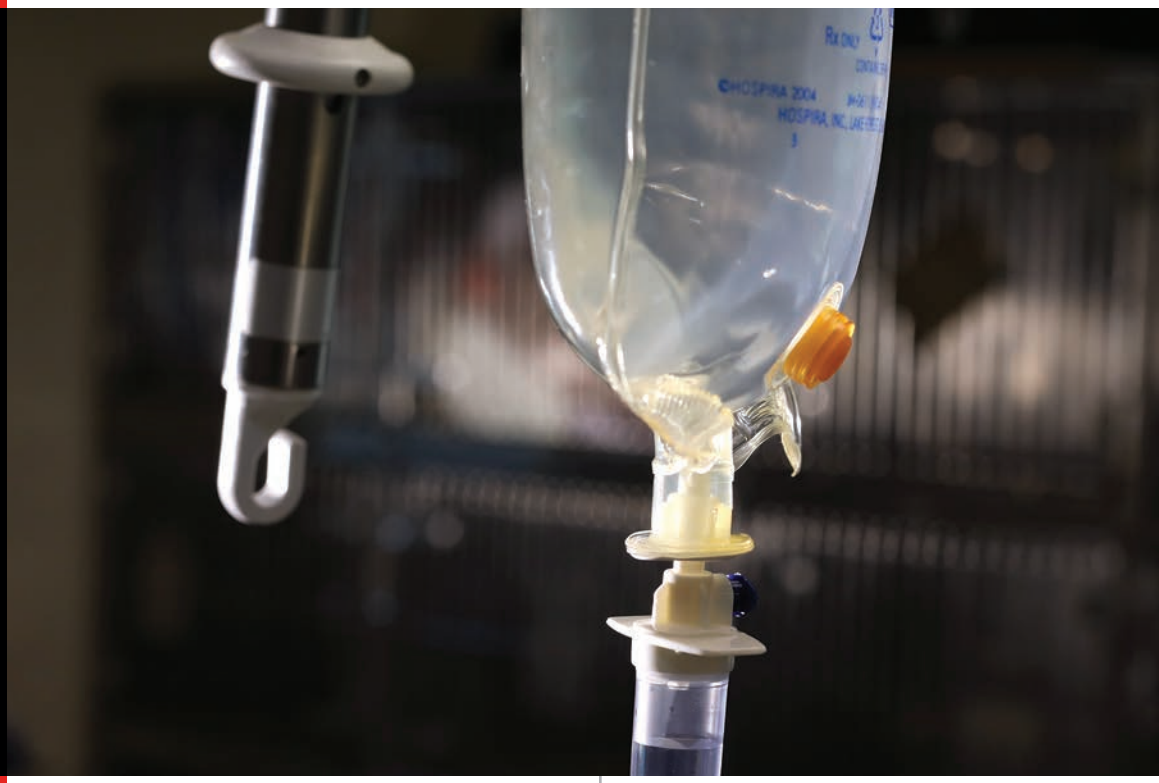

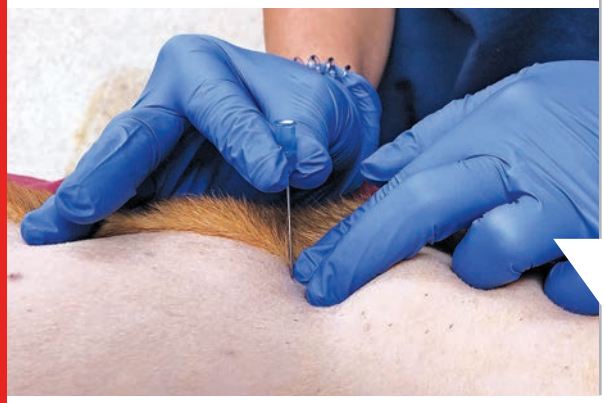


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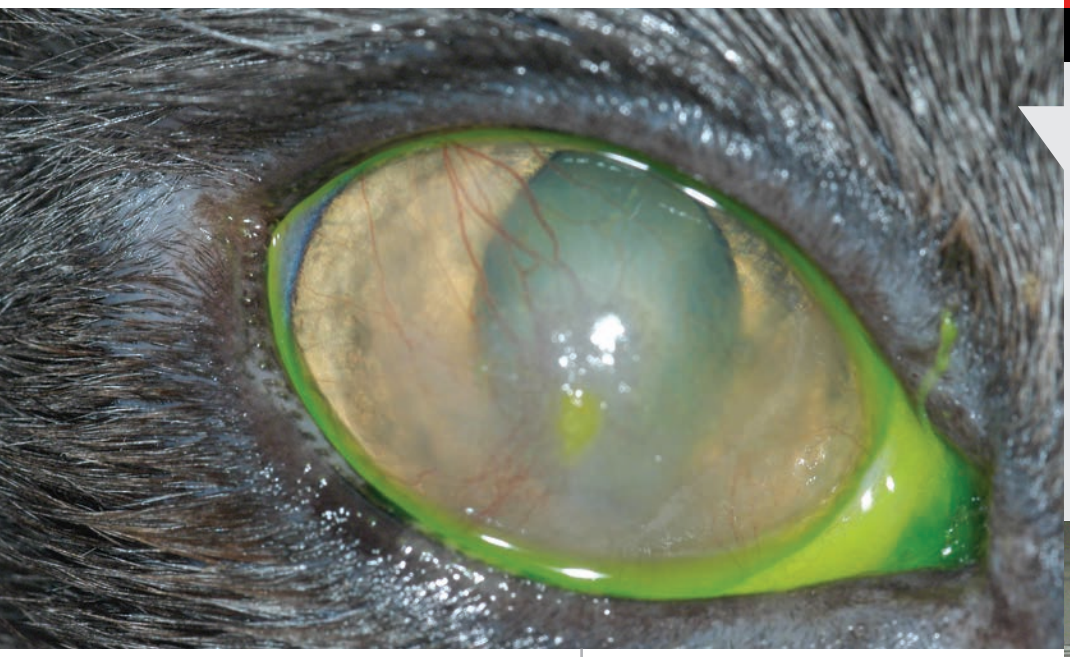

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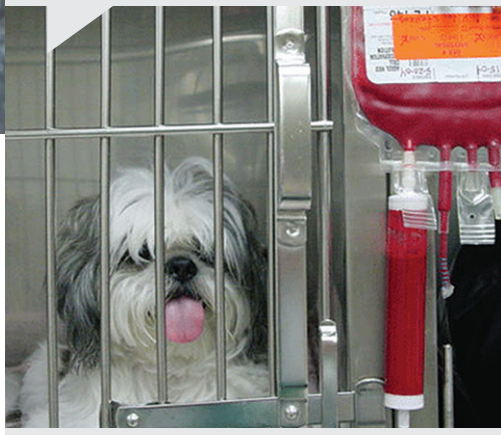

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OUR AUTHORS

TODD ARCHER, DVM, MS, DACVIM, is an associate professor of small animal internal medicine at Mississippi State University, where he also earned his DVM and master's degree and completed an internship and residency in small animal internal medicine. Dr. Archer's clinical interests include hematology, immunology, and endocrinology.

TOP 5 PAGE 35

KATHERINE BENNETT, DVM, is an anesthesia resident at University of Tennessee. She earned her DVM from Purdue University. Dr. Bennett's interests include facilitating stress-free and pain-free hospital stays for patients, learning and teaching, and presenting customized CE lectures at conferences and private clinics.

PROCEDURES PRO PAGE 62

ALISON CLODE, DVM, DACVO, is an ophthalmologist at Port City Veterinary Referral Hospital in Portsmouth, New Hampshire. Dr. Clode earned her DVM from Washington State University. She has authored multiple journal articles and book chapters on ocular pharmacotherapy and has lectured nationally and internationally on equine and companion animal ophthalmology. Her research and clinical interests include ocular pharmacology, ocular pain management, and equine and small animal corneal diseases.

CASE ROUTES PAGE 17

CHRISTINE EGGER, DVM, MVSc, CVA, CVH, DACVAA, is a professor at University of Tennessee. She earned her DVM and master's degree from University of Saskatchewan in Saskatoon, Canada. Dr. Egger completed a residency in veterinary anesthesia and is the president of the American College of Veterinary Anesthesia and Analgesia. She is certified in veterinary acupuncture and herbal medicine. Her interests include recognition and treatment of acute and chronic pain.

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SHANNA HILLSMAN, LVMT, is a senior technician in the internal medicine department at the University of Tennessee Veterinary Medical Center, where she has also worked in the intensive care unit and emergency service. She is also a blood bank technician and was a speaker at the Veterinary Partners Appreciation Conference in Knoxville, Tennessee.

DIFFERENTIAL DIAGNOSIS PAGE 29
DIFFERENTIAL DIAGNOSIS PAGE 30

Continues on page 61

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IMPORTANT SAFETY INFORMATION: ENTYCE® (capromorelin oral solution) is for use in dogs only. Do not use in breeding, pregnant or lactating dogs. Use with caution in dogs with hepatic dysfunction or renal insufficiency. Adverse reactions in dogs may include diarrhea, vomiting, polydipsia, and hypersalivation. Should not be used in dogs that have a hypersensitivity to capromorelin. Please see the full Prescribing Information at entyce.aratana.com/PI.

See page 10 for product information summary.

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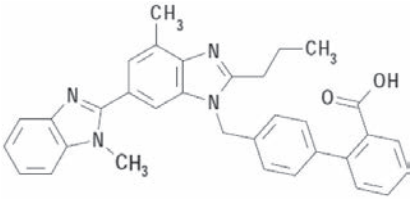
Semintra®
(telmisartan oral solution)

Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

Description: SEMINTRA (telmisartan oral solution) is a clear, colorless to yellowish viscous solution containing 10 mg/mL telmisartan. Telmisartan is an orally active, non-peptide, selective angiotensin II subtype 1 (AT1) receptor blocker. The chemical name of telmisartan is 4'-[(1,4'-dimethyl-2'propyl[2,6'-bi-1H-benzimidazol]-1'-yl)methyl]-[1,1'-biphenyl]-2-carboxylic acid. Its empirical formula is C33H30N4O2, its molecular weight is 514.63, and its structural formula is:



Indication: SEMINTRA is indicated for the control of systemic hypertension in cats.

Dosage and Administration: Always providethe Client Information Sheet with each prescription.

The initial dose of SEMINTRA is 1.5 mg/kg (0.68 mg/lb) orally twice daily for 14 days, followed by 2 mg/kg (0.91 mg/lb) orally once daily. The dose may be reduced by 0.5 mg/kg (0.23 mg/lb) increments to a minimum of 0.5 mg/kg (0.23 mg/lb) orally once daily to manage SEMINTRA-induced hypotension.

SEMINTRA can be administered directly into the mouth, or next to or on top of a small amount of food. Do not mix into food. SEMINTRA should be administered using the dosing syringe provided in the package. The dosing syringe fits onto the bottle and has 0.1 mL incremental marks. The dose should be rounded to the nearest 0.1 mL. After administration close the bottle tightly with the cap. Rinse the dosing syringe with water and let air dry.

If the cat vomits within 30 minutes of dosing, the cat may be re-dosed.

Information for Cat Owners

Always provide the Client Information Sheet with each prescription and review it with the cat owner. Advise cat owners that adverse reactions can occur with use of SEMINTRA. The most common adverse reactions reported during the field studies included vomiting, diarrhea, lethargy, weight loss, anemia and dehydration.

Contraindications: Do not use in cats with a hypersensitivity to telmisartan.

Human Warnings: Not for human use. Keep out of reach of children.

SEMINTRA is an angiotensin II antagonist/angiotensin receptor blocker (ARB). Pregnant women should avoid contact with SEMINTRA because substances that act on the renin-angiotensin-aldosterone system (RAAS) such as angiotensin receptor blockers (ARBs) can cause fetal and neonatal morbidity and death during pregnancy in humans.

Precautions: SEMINTRA has not been evaluated in cats with systolic blood pressure >200 mm Hg.

SEMINTRA can cause mild anemia or nonregenerative anemia. Cats should be monitored for anemia when initiating treatment with SEMINTRA.

SEMINTRA may cause inappetence and weight loss in some cats. Cats should be monitored for weight loss when initiating treatment with SEMINTRA. Use with caution in cats with a history of vomiting, inappetence or weight loss.

The safe use of SEMINTRA in cats with hepatic disease has not been evaluated. SEMINTRA is metabolized by the liver.

The safe use of SEMINTRA has not been evaluated in cats less than 9 months of age.

The safe use of SEMINTRA has not been evaluated in cats that are pregnant, lactating, or intended for breeding. See Human Warnings.

The safe use with other anti-hypertensive medications has not been evaluated.

Adverse Reactions:

28-day Field Effectiveness Study Safety was evaluated in a 28-day field study in 288 cats (192 SEMINTRA group cats, 96 control group cats) that received at least one dose of study drug. The control product was a vehicle control without telmisartan. Cats enrolled in the study had a median age of 14 years (7-20 years), and weighed 1.93-11.4 kg. SEMINTRA was administered orally at 1.5 mg/kg twice daily for 14 days, then 2 mg/kg once daily until study end; the control was administered at a volume equivalent to SEMINTRA. One hundred fourteen (59.4%) SEMINTRA group cats and 42 (43.8%) control group cats had at least one adverse reaction. Adverse reactions that occurred in at least 5% of either treatment group are presented in Table 1 below.

Table 1 Adverse Reactions in the 28-Day Field Study[a]

Clinical Sign	SEMINTRA N=192	Control N=96
Vomiting	46 (24.0%)	14 (14.6%)
Diarrhea	18 (9.4%)	4 (4.2%)
Lethargy	13 (6.8%)	3 (3.1%)
Weight loss	13 (6.8%)	5 (5.2%)
Decreased appetite/ Inappetence	13 (6.8%)	7 (7.3%)
Non-regenerative anemia	11 (5.7%)	2 (2.1%)
Dehydration	10 (5.2%)	4 (4.2%)
Retinal lesions (target organ damage)	4 (2.1%)	6 (6.3%)

Additional adverse reactions that occurred in <5% of the SEMINTRA group included (in order of decreasing frequency): anorexia, gagging, arrhythmia, cough, heart murmur, and regenerative anemia. Additional adverse reactions representing 2-5% of the control group included azotemia, not drinking and renal failure.

Seven cats (five SEMINTRA and two control) either died or were euthanized during the study. None of the SEMINTRA group deaths were considered related to treatment.

5-month Field Effectiveness and Safety Study

The long-term safety of SEMINTRA was evaluated in an open label, 5 month field effectiveness and safety study in 107 cats that received at least one dose of SEMINTRA. Cats enrolled in the study had a mean age of 14.1 years (7-20 years) and weighed 1.92- 11.4 kg. SEMINTRA was administered orally at 2 mg/kg once daily. Ninety-four cats (87.9%) had at least one adverse reaction during the study. Adverse reactions that occurred in at least 5% of cats are presented in Table 2 below.

Table 2 Adverse Reactions in the 5-Month Study[a]

Clinical Sign	SEMINTRA N = 107
Weight loss	37 (34.6%)
Vomiting	32 (29.9%)
Dehydration	18 (16.8%)
Non-regenerative anemia	17 (15.8%)
Anorexia	14 (13.1%)
Diarrhea	12 (11.2%)
Lethargy	12 (11.2%)
Decreased appetite/ Inappetence	11 (10.3%)
Heart murmur	10 (9.3%)
Death, Euthanasia, Found dead	9 (8.4%)
Cough	8 (7.5%)
Retinal lesions (target organ damage)	6 (5.6%)

Adverse reactions representing <5% of the study population were (in order of decreasing frequency): elevated liver enzymes, renal failure, tachycadia, arrhythmia, azotemia, depression, loose stool, constipation, gagging, hypotension, regenerative anemia, renal insufficiency, and vocalization.

Nine cats died or were euthanized during the study. Three cats had progressive chronic kidney disease that may have been affected by telmisartan treatment, concurrent disease, or inadequate control of hypertension.
The other six cats died of causes unrelated to treatment (e.g. neoplasia).

To report suspected adverse drug events, for technical assistance, or to obtain a copy of the Safety Data Sheet (SDS), contact Boehringer Ingelheim Vetmedica, Inc. at 1-866-638-2226. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or at http://www.fda.gov/AnimalVeterinary/SafetyHealth.

Clinical Pharmacology: Telmisartan is a selective angiotensin II subtype AT1 receptor blocker, with no relevant affinity for other receptors in general receptor-binding assays. Telmisartan is metabolized to the 1-Oacylglucuronide of telmisartan, which, in cats treated for 6 days at 1 mg/kg, was shown to be present in the plasma at levels approximately 21% of that of unchanged parent compound.

Following an oral dose of 1 mg/kg telmisartan once daily for five days, the time to reach mean peak plasma concentration (Tmax) was 21 minutes and 32 minutes for fasted and fed cats, respectively. There was a higher systemic exposure to telmisartan in the fasted cats based on the maximum concentration (Cmax) and area under the concentration vs time curve (AUC). The mean terminal elimination half-life was approximately 8 hours. The mean systemic exposure of telmisartan (Cmax and AUC) was approximately 60% lower for female cats compared to male cats. However, dose adjustment for female cats is not necessary. An increase in dose from 1 to 5 mg/kg once daily resulted in a greater than proportional increase in telmisartan exposure. There could be low to moderate accumulation of drug upon repeated once daily or twice daily administrations of 1.5-2 mg/kg.

Effectiveness: Effectiveness was demonstrated in a 28-day multi-center, controlled, randomizedand masked field study in client-owned cats with hypertension, and in an open label 5-month field study.

28-Day Field Study

In the 28-day study, 288 cats with hypertension (systolic blood pressure [SBP] 160-200 mmHg) were enrolled in the study and randomized to treatment with SEMINTRA (telmisartan oral solution) (n=192) or vehicle control (n=96).

Table 3 Distribution of Cats by SBP Range and Study Day in the 5-Month Study[a]

SBP Range (mm Hg)	Baseline N=107 n (%)	Day 28 N=107 n (%)	Day 56 N=102 n (%)	Day 98 N=91 n (%)	Day 140 N=80 n (%)	Day 182 N=69 n (%)
≤ 150	0(0%)	58 (54.2%)	55 (53.9%)	61 (67%)	44 (55%)	41 (59.4%)
>150-160	4 (3.7%)	19 (17.8%)	19 (18.6%)	17 (18.7%)	21 (26.2%)	16 (23.2%)
>160-170	38 (35.5%)	18 (16.8%)	14 (13.7%)	10 (11%)	12 (15%)	7 (10.1%)
>170-180	28 (26.2%)	12 (11.2%)	10 (9.8%)	2 (2.2%)	3 (3.8%)	4 (5.8%)
> 180	37 (34.6%)	0 (0%)	4 (3.9%)	1 (1.1%)	0 (0%)	1 (1.5%)

[a] SBP obtained at unscheduled visits are not represented. Cats that were removed for missing >3 doses prior to SBP measurement are not included.

The study population included cats with hypertension associated with chronic kidney disease or controlled hyperthyroidism, or idiopathic hypertension. The per protocol population for effectiveness was 141 SEMINTRA treated cats and 79 control cats. SEMINTRA was administered orally at 1.5 mg/kg twice daily for 14 days, then 2 mg/kg once daily until study end; the vehicle control was administered at a mL/kg volume equivalent to SEMINTRA. The two primary variables for effectiveness were comparison of the SEMINTRA and control group mean SBP (mSBP) from baseline to Day 14, and a decrease in mSBP >20 mmHg in the SEMINTRA group from baseline to Day 28. Cats with SBP >180 mmHg at Days 14 or 28 were rescued and removed from the study. There was a statistically significant difference between the mSBP for the SEMINTRA group compared to the control group at Day 14 (p=0.0005). At Day 14 the SEMINTRA group mSBP decreased by 23.2 mmHg, and the control group mSBP decreased by 7.3 mmHg. At Day 28, the SEMINTRA group mSBP decreased 23.9 mmHg compared to baseline.

5-Month Field Study

One hundred-seven cats from the SEMINTRA group that had successfully completed the 28-day study were enrolled in a 5-month open label study. At the beginning of the 5-month study most cats were administered SEMINTRA at 2 mg/kg once daily. Cats that experienced hypotension (defined as SBP <120 mmHg) at 2 mg/kg once daily could have the SEMINTRA dose reduced to 1 mg/kg once daily. Cats that experienced hypotension at 1 mg/kg once daily could have the SEMINTRA dose reduced again to 0.5 mg/kg once daily. Cats were evaluated for SBP, target organ damage (TOD; primarily assessed by retinal photographs), clinical pathology and adverse reactions. SBP was measured on Days 28, 56, 98, 140 and 182 and retinal photographs and clinical pathology were collected on Days 28, 98 and 182. Seventy-three (68.2%) cats completed the study (Day 182), 8 cats were removed for hypertension (SBP >180 mmHg), 2 cats were removed for hypotension, 10 cats were removed by the owner or for owner noncompliance, 8 cats were removed for new or worsening TOD, and 6 cats were removed for adverse reactions unrelated to TOD. Twenty-six cats had dose reductions to 1 mg/kg once daily to manage hypotension. Of these 26 cats, 10 had an additional dose reduction to 0.5 mg/kg once daily.

The most commonly used concomitant treatments during the 5-month study included (in order of frequency) antibiotics, anesthesia/sedatives/ analgesia, nutritional supplements, vaccines, prescription diets, antiparasitics, thyroid treatment, antiemetics and fluid therapy.

Animal Safety: In a six-month target animal safety study, healthy cats 9 to 13 months old were administered telmisartan orally, once daily at 0, 1, 3, or 5 mg/kg body weight.

Control cats (0 mg/kg) received saline at a volume equal to the 5 mg/kg dose. There were eight cats per group (4 males, 4 females).

All cats survived the study, and there were no telmisartan-related effects on clinical observations, physical examination, body weight, ophthalmic examination, coagulation parameters, urinalysis, and gross necropsy.

Blood pressure was lower in the groups administered telmisartan compared to the control group. Blood pressure was lower starting at week 4 in the 1 mg/kg group, at week 2 in the 3 mg/kg group, and during the first week in the 5 mg/kg group. This is an expected pharmacologic effect of telmisartan. Food consumption in the 3 and 5 mg/kg group cats was lower than that of the control group.

Telmisartan-related effects on hematology parameters included lower red blood cell count, hemoglobin, hematocrit, and reticulocytes in the 3 and 5 mg/kg group cats. One 5 mg/kg group cat also had mild generalized depletion of the hematopoietic cells on bone marrow histology. In some 5 mg/kg group cats, decreases in red blood cell precursors on bone marrow cytology were considered telmisartan-related.

Blood urea nitrogen (BUN) was statistically significantly higher for the 3 mg/kg group at weeks 12 and 16, and for the 5 mg/kg group at weeks 2, 4, 7, 12, 16, 20, and 25, when compared to the control group. There were no clinical signs associated with the changes in BUN.

There was a telmisartan-related effect on lower heart weight in the 3 and 5 mg/kg groups compared to the control group, but the histopathology was normal in all treated cats. On kidney histology, there was minimal to mild hypertrophy of the juxtaglomerular apparatus in the 1, 3, and 5 mg/kg group cats. Kidney histology was normal in control group cats.

Storage Conditions: Store at or below 25°C (77°F) with excursions permitted up to 40°C (104°F). Once the bottle is opened, use the contents within six months.

How Supplied: SEMINTRA (telmisartan oral solution), 10 mg/mL, 35 mL fill volume, is supplied in a 45 mL plastic bottle with a dosing syringe.
NDC 0010-4492-01

NADA 141-501, Approved by FDA

Manufactured for:
Boehringer Ingelheim Vetmedica, Inc.
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INTRODUCING

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- Easy-to-use syringe allows for accurate dosing and flexible dosing[2]
- Safe for long-term administration, with once-daily dosing after 14 days[1]

IMPORTANT SAFETY INFORMATION

SEMINTRA is an angiotensin II antagonist/angiotensin receptor blocker (ARB). Pregnant women should avoid contact with SEMINTRA because it can cause fetal and neonatal morbidity and death during pregnancy in humans. Pregnant women should avoid contact with SEMINTRA because other similar drugs have been found to harm the unborn baby during pregnancy. **Precautions:** SEMINTRA can cause mild anemia or non-regenerative anemia. Cats should be monitored for anemia when initiating treatment. Cats should be monitored for weight loss when initiating treatment with SEMINTRA. Use with caution in cats with a history of vomiting, inappetence or weight loss. The safe use of SEMINTRA in cats with hepatic disease has not been evaluated. SEMINTRA is metabolized by the liver. SEMINTRA has not been evaluated in cats with systolic blood pressure > 200 mmHg. The safe use of SEMINTRA has not been evaluated in cats less than 9 months of age, or in cats that are pregnant, lactating, or intended for breeding.
The safe use with other anti-hypertensive medications has not been evaluated.
For additional information, see the full prescribing information on page 12.

References: 1. Semintra® (telmisartan oral solution) Prescribing Information. Boehringer Ingelheim Vetmedica, Inc. 2018.
2. Zimmering T. Ease of use of Semintra® and its effects on quality of life—update on cat owner feedback ("EASY Programme") [abstract]. In: Proceedings from the 21st Federation of European Companion Animal Veterinary Associations (FECAVA); October 15–17, 2015; Barcelona, Spain. Poster.

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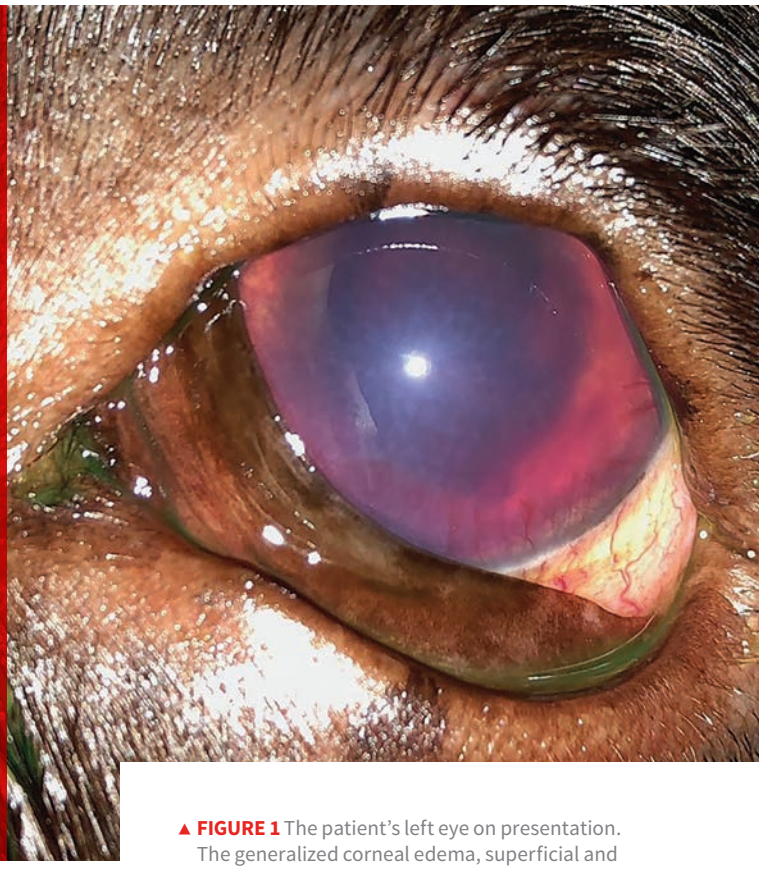
Hemorrhagic Anterior Uveitis in a Labrador Retriever

Alison Clode, DVM, DACVO
Port City Veterinary Referral Hospital
Portsmouth, New Hampshire



▲ **FIGURE 1** The patient's left eye on presentation. The generalized corneal edema, superficial and deep peripheral corneal vascularization, and intraocular hemorrhage, with a visible but difficult to visualize pupil, are evident.

THE CASE

Sammy, a 9-year-old neutered male Labrador retriever, is presented for evaluation of a red, cloudy, painful left eye. The abnormal appearance to the eye was noted by the owners after Sammy had been left to play unattended with the other dog in the household for approximately 2 hours. No treatment was administered by the owners, and Sammy was presented 45 minutes after the owners first noted the abnormality.

On examination, Sammy is bright, alert, and responsive. The left eye is blepharospastic, with mild swelling of the eyelids, conjunctival hyperemia, corneal edema, hyphema, and superficial and deep peripheral corneal vascularization (***Figure 1***). The pupil is difficult to visualize but appears miotic as compared with the right eye. Direct pupillary light reflex (PLR) is absent, and consensual PLR in the right eye is present but subjectively decreased. Dazzle reflex (ie, reflex reaction to stimulation of the eye by a bright light) is positive, but menace response is negative in the left eye. Menace response, direct PLR, and dazzle reflex are positive in the right eye, but consensual PLR in the left eye is difficult to visualize due to hyphema in the left eye. Schirmer tear test shows >15 mm wetting/min in both eyes, fluorescein stain is negative in both eyes, and intraocular pressure (IOP), estimated by applanation tonometry, is 14 mm Hg in the right eye and 6 mm Hg in the left. The remainder of the ocular examination in the right eye, including fundic examination, is normal.

What are the next steps?

THE CHOICE IS YOURS ...

CASE ROUTE 1

To diagnose the patient with presumptive hemorrhagic anterior uveitis secondary to trauma in the left eye and treat for anterior uveitis, go to page 18.

CASE ROUTE 2

To diagnose the patient with hemorrhagic anterior uveitis of unknown etiology in the left eye and perform additional diagnostics, go to page 20.

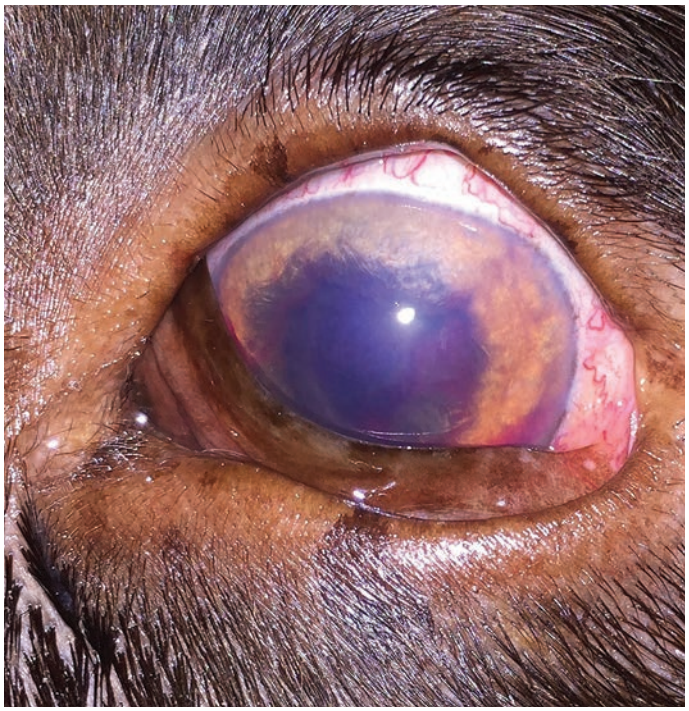
IOP = intraocular pressure
PLR = pupillary light reflex

CASE ROUTE 1

You elect to diagnose the patient with presumptive hemorrhagic anterior uveitis secondary to trauma in the left eye and treat for anterior uveitis.

Case Progression

Because of Sammy's acute onset of ocular changes, trauma is suspected as the cause of intraocular bleeding. Because trauma is a one-time occurrence, treatment is targeted toward controlling intraocular inflammation associated with bleeding and managing discomfort. Administration of a topical ophthalmic antibiotic–corticosteroid combination (eg, neomycin–polymyxin B–dexamethasone ophthalmic solution [1 drop in the left eye q12h]) is initiated to control intraocular inflammation, and analgesia is provided through oral NSAIDs. Recheck examination is scheduled for 3 to 5 days later.



▲ **FIGURE 2** The patient's left eye on recheck examination 5 days after initial presentation. The corneal edema has improved, with less free-floating blood and more discrete clotting around the dyscoric pupil.

On recheck examination performed 5 days following initial presentation, the owners report that Sammy became significantly more comfortable in the first 1 to 2 days following initial presentation but began squinting and rubbing the left eye a day before the recheck examination. Blepharospasm is present in the eye. The corneal edema has improved, with less free-floating blood and more discrete clotting around the dyscoric pupil (***Figure 2***). The pupil is miotic and irregularly shaped (ie, dyscoric), with irregular bulging and thickening of the surrounding iris. IOP is 43 mm Hg, and menace response, direct PLR, dazzle reflex, and consensual PLR in the right eye (resulting from shining light in the left eye) are absent. The ocular examination remains normal in the right eye.

Clinical diagnoses include hyphema with an intraocular blood clot, secondary glaucoma, and blindness in the left eye. Determining the prognosis for regaining vision is difficult; however, the owners' report of Sammy's squinting and rubbing the eye for at least a day (potentially indicating glaucoma of a day's duration), lack of a consensual PLR in the right eye in response to shining light in the left eye, and lack of dazzle reflex in the left eye are suggestive of a poor prognosis for regaining vision.[1] More aggressive intervention is advised to improve comfort while minimizing the intensiveness of medical therapy.

Clinical Considerations

Options for intervention include evisceration (ie, replacement of the intraocular contents with an implant while preserving the cornea, sclera, extraocular muscles, and adnexa), enucleation (ie, surgical removal of the entire globe), or gentamicin (25-50 mg injected into the vitreous) to destroy

the ciliary body, thus decreasing production of aqueous humor and lessening dependence on medications to control secondary glaucoma.

Outcome

Intraocular injections may be contraindicated in eyes with pre-existing ocular hemorrhage due to the potential increase in hemorrhage, and evisceration is primarily performed for cosmetic reasons. Thus, enucleation is elected in this patient and performed under general anesthesia. The globe is submitted for histopathology, and the findings are consistent with intraocular hemorrhage and glaucoma and are identified as secondary to an infiltrative, neoplastic iridal lesion.

Your Choice's Implications

Although treatment with a topical corticosteroid and an oral NSAID is appropriate to control inflammation and pain in cases of presumed traumatic anterior uveitis, additional diagnostic procedures (see ***Case Route 2***, next page) should be appropriately performed on any eye with hyphema to rule out other possible causes of bleeding. If performing additional diagnostic procedures is not possible, more aggressive treatment, such as a topical corticosteroid with greater intraocular penetration (eg, prednisolone acetate 1%),[2] may be more effective in producing a favorable outcome if trauma—or another one-time, controllable condition—is the cause. In addition, because the need for antibiotics is low in patients with intraocular hemorrhage (as represented in the neomycin–polymyxin B–dexamethasone combination), avoiding unnecessary antimicrobial use is recommended. If neomycin–polymyxin B–dexamethasone is the only medication readily available, increasing the frequency of administration (ie, to q6-8h) may be helpful as more aggressive initial treatment. Owner education is also a critical component of the treatment plan, as owners should be aware of the signs (eg, squinting, rubbing, increased cloudiness, increased redness) that would indicate that earlier re-evaluation is necessary.

Treatment with a mydriatic cycloplegic (eg, atropine ophthalmic solution 1%) is indicated in patients with anterior uveitis and low IOP, even if the pupil cannot be visualized due to signs caused by the disease process. Because anterior uveitis produces a miotic, "sticky" pupil, the risk for complete posterior synechiae—and thus secondary glaucoma—is decreased by the use of atropine, which produces pupillary dilation, decreases exudation from the iris, and provides analgesia via cycloplegia. When surgical removal of a globe is advised to treat a painful ocular disease (eg, glaucoma) and the underlying cause of the disease (eg, intraocular tumor) has not been identified, histopathology is appropriate, as the patient's well-being may be positively impacted if a previously occult disease process is identified.

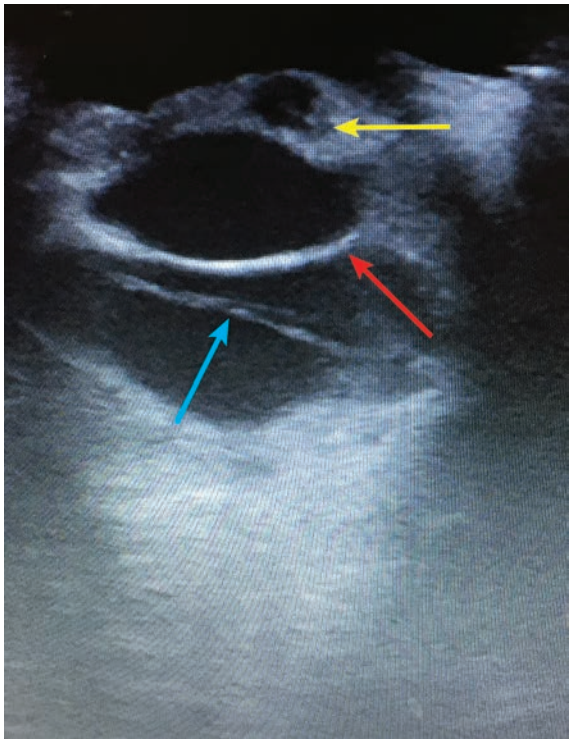
In this case progression, if additional diagnostics—particularly ocular ultrasonography—had been performed at initial presentation, medical management for the intraocular hemorrhage would have been recognized as ineffective treatment for the underlying cause ultimately identified (ie, intraocular tumor). Because ocular ultrasonography may not be performed on all patients with hyphema for various reasons, it is important to consider that more aggressive medical management is appropriate, in the event that anterior uveitis is medically responsive.

Intraocular injections may be contraindicated in eyes with pre-existing ocular hemorrhage due to the potential increase in hemorrhage.

IOP = intraocular pressure
PLR = pupillary light reflex

CASE ROUTE 2

Based in part on the presence of deep peripheral corneal vascularization, you are suspicious of a more chronic intraocular disease process. You elect to diagnose the patient with hemorrhagic anterior uveitis of unknown etiology in the left eye and perform additional diagnostics.



▲ **FIGURE 3** Ultrasonographic image of the patient's left eye obtained on initial presentation. The cornea is near the top of the image, and the sclera is toward the bottom of the image, with the posterior lens capsule (***red arrow***) visible. Retinal detachment (***blue arrow***) is visible as a hyperechoic line in the vitreal space, and the cavitary lesions of the iris (***yellow arrow***) are present anterior to the posterior lens capsule.

Case Progression

Other conditions that may lead to intraocular hemorrhage, such as those localized to the eye (eg, trauma, retinal detachment, intraocular tumor), as well as those with systemic involvement (eg, systemic hypertension, coagulopathy, vasculitis, systemic infections, systemic neoplasia), are considered.[3] Thus, based on the diagnosis of hemorrhagic anterior uveitis and the inability to visualize intraocular structures, additional diagnostics are performed to confirm the underlying cause of the bleeding. These diagnostic tests are ordered to noninvasively and cost-effectively provide the most high-yield information based on signalment and clinical signs.

General physical examination parameters are within normal limits. Systemic blood pressure obtained via Doppler averages 110 mm Hg (systolic). CBC, serum chemistry profile, coagulation testing, and urinalysis results are normal. Further tests to evaluate for systemic inflammatory and neoplastic conditions (eg, infectious disease titers, chest and abdominal imaging) are not performed, and further ocular evaluation is pursued.

Following administration of a topical local anesthetic (ie, proparacaine ophthalmic solution [2 drops administered 3-5 minutes apart]), ocular ultrasonography is performed with a 12-MHz transducer placed transcorneally in transverse and sagittal orientations using sterile lubricating jelly.[4] Although visualization of the anterior segment is less clear with this probe than would be achieved with a higher-frequency probe, multifocal cavitations within the iris architecture, as well as complete retinal detachment (***Figure 3***), are identified.

Based on the signalment, general physical examination findings, and additional diagnostic tests and procedures, diagnoses of hemorrhagic anterior uveitis and retinal detachment secondary to a suspected iridal tumor are made.

Clinical Considerations

Because the likelihood of controlling intraocular hemorrhage and regaining vision are poor based on the underlying disease process, surgical removal of the eye and submission for histopathologic evaluation are recommended.

Outcome

Enucleation of the left eye is performed, and the globe is submitted for histopathologic evaluation. A diagnosis of iridal hemangiosarcoma, with retinal detachment and intraocular hemorrhage, is made. Radiography of the chest and abdominal ultrasonography are performed to determine if metastatic disease is present, and the findings are normal.

Your Choice's Implications

Evaluating the patient for disease processes potentially associated with intraocular hemorrhage was appropriate to determine the prognosis and effective therapies. Ocular ultrasonography was the most informative diagnostic procedure performed and allowed for appropriate intervention to be performed at an early stage in the ocular disease process. Radiographic imaging (eg, chest radiography, abdominal ultrasonography or radiography) may also be considered preoperatively to determine the overall systemic condition prior to surgical intervention. If not performed preoperatively, as in this case, radiographic imaging can be performed postoperatively if histopathology results indicate.

References

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4. Dietrich UM. Ophthalmic examination and diagnostics. In: Gelatt KN, Gilger BC, Kern TJ, eds. *Veterinary Ophthalmology*. 5th ed. Ames, IA: Wiley-Blackwell; 2013:669-683.

Cardiology on a Budget

When the cost of cardiac diagnostic testing must be limited, considering whether a test will change the course of treatment can help prioritize which tests to perform. For example, if an arrhythmia is present, thoracic radiography and echocardiography are superior to electrocardiography for determining heart size.

In subclinical dogs, delaying advanced imaging may be considered. In small-breed dogs with a signalment and murmur consistent with degenerative valve disease, advanced imaging can be delayed until the murmur is at least grade 3/6. Echocardiography in dogs allows clinicians to determine when to initiate pimobendan therapy, based on EPIC study criteria. In patients with congestive heart failure, annual echocardiography may be ideal to diagnose comorbidities such as pulmonary hypertension; however, without new signs suggestive of additional clinical problems, it is unlikely echocardiography or radiography will result in changes to treatment plans.

Although echocardiography is the only test that will allow definitive diagnosis of underlying types of heart disease in cats, radiography and/or NT-proBNP testing can also provide useful information and are reasonable screening tests. Cardiac silhouette in cats is often normal in early myocardial disease when left ventricular thickening is present without left atrial enlargement. Cardiac medications are generally not indicated in cats until there is moderate left atrial enlargement. In addition, some owners may not be able to effectively administer medications and may choose not to medicate. In such situations, there is no benefit to identifying underlying disease; thus, home-monitoring for signs of congestive heart failure become important. Because of the uncertain efficacy of compounded pimobendan, this drug is only recommended in cats in extenuating circumstances; alternative medications for heart failure should be considered.—*Sleeper M*

Medical Cannabis for Pain

The endocannabinoid system (ECS) is an extensive group of endogenous cannabinoid receptors located both centrally and peripherally in nearly all vertebrates. Since 1992, 5 endogenous cannabinoids (ie, internally produced agonists of the ECS) have been isolated; this discovery lends validation to the evaluation of the ECS and how the use of pharmaceuticals such as medical cannabis may be an important tool for treating many conditions, including acute, chronic, neuropathic, and visceral pain.

Phytocannabinoids are chemical compounds extracted from marijuana or hemp plants that act on the ECS, and their use in veterinary medicine has been growing rapidly, despite a dearth of animal studies supporting appropriate dosing, efficacy, and safety. Cannabidiol (CBD) is the focus of several ongoing safety and efficacy studies. CBD is thought to work at the CB1 and CB2 receptors of the ECS, affecting pain modulation and helping prevent the natural breakdown of the endogenous cannabinoid anandamide, thereby creating a synergistic effect. Other responses, such as the inhibition of proinflammatory cytokine production and the release of anti-inflammatory cytokines, have also been observed. Preliminary data show limited side effects, with diarrhea and elevation in alkaline phosphatase being most common.—*Cital S*

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Important Safety Information

Mirataz™ (mirtazapine transdermal ointment) is for topical use in cats only under veterinary supervision. Do not use in cats with a known hypersensitivity to mirtazapine or any of the excipients. Do not use in cats treated with monoamine oxidase inhibitors (MAOIs). Not for human use. Keep out of reach of children. Wear gloves when handling/applying, wash hands after and avoid contact between the treated cat and people or other animals for 2 hours following application. Use with caution in cats with hepatic and kidney disease. Cat's food intake should be monitored upon discontinuation. Safety has not been evaluated in cats less than 2 kg, less than six months of age or in breeding, pregnant or lactating cats. The most common adverse reactions observed during clinical trials were application site reactions, behavioral abnormalities (vocalization and hyperactivity) and vomiting. **For additional safety information, see brief summary of prescribing information on page 21.**

Reference: 1. Mirataz™ (mirtazapine transdermal ointment) [package insert], Kindred Biosciences, Inc. (Burlingame, CA). Rev. 5/2018. **2.** Buhles W, Quimby JM, Labelle D, et al. Single and multiple dose pharmacokinetics of a novel transdermal ointment in cats. J Vet Pharmacol Ther. In press 2018.

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Anesthetizing Older Cats

Many older cats require anesthesia for various reasons (eg, dental procedures), and age-related anesthetic requirements are of great importance, as cats older than 12 years, independent of health status, have been shown to have double the risk for anesthetic death as compared with cats 6 months to 5 years of age. Physiologic changes can alter pharmacokinetics, and significant changes in renal and hepatic function may not be evident on routine blood work. Cardiac dysfunction may be subclinical as well.

Preoxygenation is recommended in older patients, as they are more susceptible to hypoxia and hypercapnia. NSAIDs can worsen renal blood perfusion because of prostaglandin release; thus, it is critical to prevent, recognize, and treat hypotension if these drugs are used. Age-related decreases in brain mass reduce inhaled anesthetic requirements in humans. Because the same is assumed to be true in cats, anesthetic depth should be closely monitored. Various age-related changes, including alterations in body composition and metabolism, can result in unpredictable drug effects.

Complete history and physical examination, routine blood work, and other diagnostic testing based on clinical findings are recommended. Premedication is crucial to lessen patient stress and resulting deleterious effects on cardiac and renal function and perfusion due to catecholamine release. Judicious acepromazine administration has antinausea and antiarrhythmia benefits, as well as anesthetic-sparing activity (as do opioids). Benzodiazepines are good sedatives and are reversible, should an adverse event occur. Ketamine and propofol are additional drugs that can be beneficial in older cats if used judiciously. In addition, locoregional blocks decrease the need for inhaled anesthetics and can improve patient comfort postoperatively. Because most anesthetic deaths occur in the postoperative period, monitoring and supportive care are crucial. Supplemental oxygen and thermal support should be provided. *—Robertson SA*

Because most anesthetic deaths occur in the postoperative period, monitoring and supportive care are crucial.

A Practical Approach to Respiratory Distress

Signalment, patient history, and physical examination can help narrow the differential list for patients in respiratory distress. Trauma patients may suffer from pneumothorax, hemothorax, and/or pulmonary contusions. The most common causes of respiratory distress in cats are congestive heart failure (CHF) and allergic bronchitis (ie, asthma). Whereas respiratory distress of many etiologies can cause tachycardia, CHF frequently causes bradycardia in cats. Auscultation may reveal a murmur and crackles. Pleural and/or pericardial effusion are often present. Allergic bronchitis is most commonly seen in younger cats with a history of nonproductive cough; these patients may be presented with wheezing with an abdominal push and exaggerated expiratory phase.

Canine signalment is especially important. In brachycephalic breeds, upper airway obstruction associated with brachycephalic airway syndrome and aspiration pneumonia should be high on the differential list. Aspiration pneumonia should be considered in any dog, especially when there is a history of vomiting. CHF, pulmonary hypertension, and tracheal collapse are common in small breeds. Breed-associated heart disease should be investigated in boxers, Cavalier King Charles spaniels, and Doberman pinschers. Older large-breed dogs are prone to laryngeal paralysis.

Patients in respiratory distress require prompt oxygen supplementation and sedation. Butorphanol (0.2-0.3 mg/kg IV or IM) has cardiovascular-sparing effects and reduces respiratory depression. Acepromazine (0.01-0.02 mg/kg IV or IM) can be used in patients that do not have cardiovascular compromise. Patients often tolerate oxygen masks better than flow-by oxygen. Nasal cannulas allow more mobility as compared with masks. Small patients can benefit from oxygen cages, and patients with life-threatening respiratory distress or upper airway obstruction or those not improving with standard therapy may require intubation.*—Culler CA*

Take a bite out of Lyme.

NEW CLAIM!

NexGard® (afoxolaner) is the only product approved by the FDA for the prevention of infections that cause Lyme disease in dogs as a result of killing black-legged ticks.

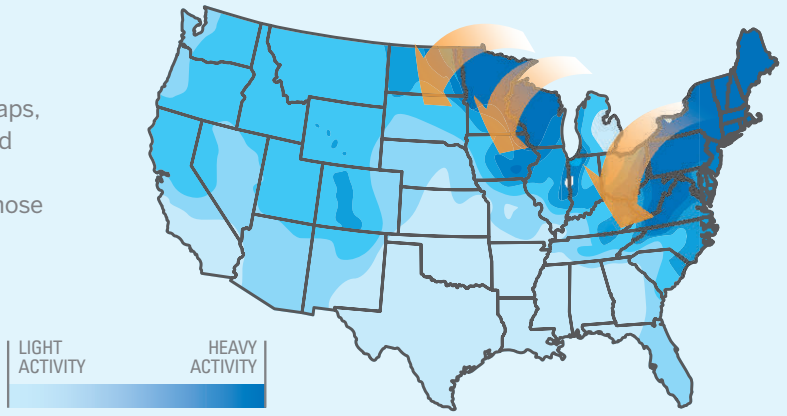
Lyme disease is spreading

According to the CAPC Parasite Prevalence maps, Lyme disease is the most commonly diagnosed tick-borne disease in dogs in the US.[1] It's a debilitating illness that can be difficult to diagnose and treat – but easy to prevent in dogs.

Straight from the CAPC:

"Nationwide, dogs exposed to the agent of Lyme disease are continuing to be discovered in areas outside recognized endemic regions."[2]

LYME DISEASE - CAPC FORECAST



Proven Results against *B. burgdorferi* transmission[3]

The ability of *NexGard* (afoxolaner) to prevent the transmission of *Borrelia burgdorferi* by killing infected ticks

- The study evaluated two groups of dogs: an untreated control group and a **NexGard**-treated group.
- The dogs in the treated group received **NexGard** on day 0.
- All dogs were:
  - Infested with ~50 adult *Ixodes scapularis* ticks (with a *B. burgdorferi* infection rate of 63.1%) on day 28.
  - Tested using Lyme Quant C6® and SNAP® 4DX® on days 48, 62, 76, 90, and 102.
  - Tested for the presence of *B. burgdorferi* DNA via PCR testing. Skin biopsies collected on day 104.

Detection of *Borrelia burgdorferi* infection	Untreated Control Group	NexGard-treated Group
Lyme Quant C6 & SNAP 4DX	ALL dogs tested positive	ALL dogs tested negative
PCR	ALL dogs tested positive	ALL dogs tested negative
		100% PROTECTED

***NexGard* is a Merial product. Merial is now part of Boehringer Ingelheim.**

Boehringer Ingelheim

IMPORTANT SAFETY INFORMATION: NexGard is for use in dogs only. The most frequently reported adverse reactions include vomiting, pruritus, lethargy, diarrhea and lack of appetite. The safe use of **NexGard** in pregnant, breeding, or lactating dogs has not been evaluated. Use with caution in dogs with a history of seizures or neurologic disorders. For more information, see the full prescribing information or visit www.NexGardForDogs.com.

NexGard®
(afoxolaner) Chewables

CAUTION: Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.

Description:
NexGard® (afoxolaner) is available in four sizes of beef-flavored, soft chewables for oral administration to dogs and puppies according to their weight. Each chewable is formulated to provide a minimum afoxolaner dosage of 1.14 mg/lb (2.5 mg/kg). Afoxolaner has the chemical composition 1-Naphthalenecarboxamide, 4-[5- [3-chloro-5-(trifluoromethyl)-phenyl]-4, 5-dihydro-5-(trifluoromethyl)-3-isoxazolyl]-N-[2-oxo-2-[(2,2,2-trifluoroethyl)amino]ethyl.

Indications:
NexGard kills adult fleas and is indicated for the treatment and prevention of flea infestations *(Ctenocephalides felis),* and the treatment and control of Black-legged tick *(Ixodes scapularis),* American Dog tick *(Dermacentor variabilis),* Lone Star tick *(Amblyomma americanum),* and Brown dog tick (*Rhipicephalus sanguineus*) infestations in dogs and puppies 8 weeks of age and older, weighing 4 pounds of body weight or greater, for one month. NexGard is indicated for the prevention of *Borrelia burgdorferi* infections as a direct result of killing *Ixodes scapularis* vector ticks.

Dosage and Administration:
NexGard is given orally once a month, at the minimum dosage of 1.14 mg/lb (2.5 mg/kg).

Dosing Schedule:

Body Weight	Afoxolaner Per Chewable (mg)	Chewables Administered
4.0 to 10.0 lbs.	11.3	One
10.1 to 24.0 lbs.	28.3	One
24.1 to 60.0 lbs.	68	One
60.1 to 121.0 lbs.	136	One
Over 121.0 lbs.	Administer the appropriate combination of chewables	

NexGard can be administered with or without food. Care should be taken that the dog consumes the complete dose, and treated animals should be observed for a few minutes to ensure that part of the dose is not lost or refused. If it is suspected that any of the dose has been lost or if vomiting occurs within two hours of administration, redose with another full dose. If a dose is missed, administer NexGard and resume a monthly dosing schedule.

Flea Treatment and Prevention:
Treatment with NexGard may begin at any time of the year. In areas where fleas are common year-round, monthly treatment with NexGard should continue the entire year without interruption.

To minimize the likelihood of flea reinfestation, it is important to treat all animals within a household with an approved flea control product.

Tick Treatment and Control:
Treatment with NexGard may begin at any time of the year (see **Effectiveness**).

Contraindications:
There are no known contraindications for the use of NexGard.

Warnings:
Not for use in humans. Keep this and all drugs out of the reach of children. In case of accidental ingestion, contact a physician immediately.

Precautions:
Afoxolaner is a member of the isoxazoline class. This class has been associated with neurologic adverse reactions including tremors, ataxia, and seizures. Seizures have been reported in dogs receiving isoxazoline class drugs, even in dogs without a history of seizures. Use with caution in dogs with a history of seizures or neurologic disorders (see **Adverse Reactions** and **Post-Approval Experience**).

The safe use of NexGard in breeding, pregnant or lactating dogs has not been evaluated.

Adverse Reactions:
In a well-controlled US field study, which included a total of 333 households and 615 treated dogs (415 administered afoxolaner; 200 administered active control), no serious adverse reactions were observed with NexGard.

Over the 90-day study period, all observations of potential adverse reactions were recorded. The most frequent reactions reported at an incidence of > 1% within any of the three months of observations are presented in the following table. The most frequently reported adverse reaction was vomiting. The occurrence of vomiting was generally self-limiting and of short duration and tended to decrease with subsequent doses in both groups. Five treated dogs experienced anorexia during the study, and two of those dogs experienced anorexia with the first dose but not subsequent doses.

Table 1: Dogs With Adverse Reactions.

	Treatment Group			
	Afoxolaner		Oral active control	
	N[1]	% (n=415)	N[2]	% (n=200)
Vomiting (with and without blood)	17	4.1	25	12.5
Dry/Flaky Skin	13	3.1	2	1.0
Diarrhea (with and without blood)	13	3.1	7	3.5
Lethargy	7	1.7	4	2.0
Anorexia	5	1.2	9	4.5

[1]Number of dogs in the afoxolaner treatment group with the identified abnormality.
[2]Number of dogs in the control group with the identified abnormality.

In the US field study, one dog with a history of seizures experienced a seizure on the same day after receiving the first dose and on the same day after receiving the second dose of NexGard. This dog experienced a third seizure one week after receiving the third dose. The dog remained enrolled and completed the study. Another dog with a history of seizures had a seizure 19 days after the third dose of NexGard. The dog remained enrolled and completed the study. A third dog with a history of seizures received NexGard and experienced no seizures throughout the study.

Post-Approval Experience (July 2018):
The following adverse events are based on post-approval adverse drug experience reporting. Not all adverse events are reported to FDA/CVM. It is not always possible to reliably estimate the adverse event frequency or establish a causal relationship to product exposure using these data.

The following adverse events reported for dogs are listed in decreasing order of reporting frequency for NexGard:

Vomiting, pruritus, lethargy, diarrhea (with and without blood), anorexia, seizure, hyperactivity/restlessness, panting, erythema, ataxia, dermatitis (including rash, papules), allergic reactions (including hives, swelling), and tremors.

Contact Information:
For a copy of the Safety Data Sheet (SDS) or to report suspected adverse drug events, contact Merial at 1-888-637-4251 or www.nexgardfordogs.com.

For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at http://www.fda.gov/AnimalVeterinary/SafetyHealth.

Mode of Action:
Afoxolaner is a member of the isoxazoline family, shown to bind at a binding site to inhibit insect and acarine ligand-gated chloride channels, in particular those gated by the neurotransmitter gamma-aminobutyric acid (GABA), thereby blocking pre- and post-synaptic transfer of chloride ions across cell membranes. Prolonged afoxolaner-induced hyperexcitation results in uncontrolled activity of the central nervous system and death of insects and acarines. The selective toxicity of afoxolaner between insects and acarines and mammals may be inferred by the differential sensitivity of the insects and acarines' GABA receptors versus mammalian GABA receptors.

Effectiveness:
In a well-controlled laboratory study, NexGard began to kill fleas four hours after initial administration and demonstrated >99% effectiveness at eight hours. In a separate well-controlled laboratory study, NexGard demonstrated 100% effectiveness against adult fleas 24 hours post-infestation for 35 days, and was ≥93% effective at 12 hours post-infestation through Day 21, and on Day 35. On Day 28, NexGard was 81.1% effective 12 hours post-infestation. Dogs in both the treated and control groups that were infested with fleas on Day -1 generated flea eggs at 12- and 24-hours post-treatment (0-11 eggs and 1-17 eggs in the NexGard treated dogs, and 4-90 eggs and 0-118 eggs in the control dogs, at 12- and 24-hours, respectively). At subsequent evaluations post-infestation, fleas from dogs in the treated group were essentially unable to produce any eggs (0-1 eggs) while fleas from dogs in the control group continued to produce eggs (1-141 eggs).

In a 90-day US field study conducted in households with existing flea infestations of varying severity, the effectiveness of NexGard against fleas on the Day 30, 60 and 90 visits compared with baseline was 98.0%, 99.7%, and 99.9%, respectively.

Collectively, the data from the three studies (two laboratory and one field) demonstrate that NexGard kills fleas before they can lay eggs, thus preventing subsequent flea infestations after the start of treatment of existing flea infestations.

In well-controlled laboratory studies, NexGard demonstrated >97% effectiveness against *Dermacentor variabilis,* >94% effectiveness against *Ixodes scapularis,* and >93% effectiveness against *Rhipicephalus sanguineus,* 48 hours post-infestation for 30 days. At 72 hours post-infestation, NexGard demonstrated >97% effectiveness against *Amblyomma americanum* for 30 days. In two separate, well-controlled laboratory studies, NexGard was effective at preventing *Borrelia burgdorferi* infections after dogs were infested with *Ixodes scapularis* vector ticks 28 days post-treatment.

Animal Safety:
In a margin of safety study, NexGard was administered orally to 8 to 9-week-old Beagle puppies at 1, 3, and 5 times the maximum exposure dose (6.3 mg/kg) for three treatments every 28 days, followed by three treatments every 14 days, for a total of six treatments. Dogs in the control group were sham-dosed. There were no clinically-relevant effects related to treatment on physical examination, body weight, food consumption, clinical pathology (hematology, clinical chemistries, or coagulation tests), gross pathology, histopathology or organ weights. Vomiting occurred throughout the study, with a similar incidence in the treated and control groups, including one dog in the 5x group that vomited four hours after treatment.

In a well-controlled field study, NexGard was used concomitantly with other medications, such as vaccines, anthelmintics, antibiotics (including topicals), steroids, NSAIDS, anesthetics, and antihistamines. No adverse reactions were observed from the concomitant use of NexGard with other medications.

Storage Information:
Store at or below 30°C (86°F) with excursions permitted up to 40°C (104°F).

How Supplied:
NexGard is available in four sizes of beef-flavored soft chewables: 11.3, 28.3, 68 or 136 mg afoxolaner. Each chewable size is available in color-coded packages of 1, 3 or 6 beef-flavored chewables.

NADA 141-406, Approved by FDA

Marketed by: Frontline Vet Labs™, a Division of Merial, Inc.
Duluth, GA 30096-4640 USA

Made in Brazil.

1050-4493-07
Rev. 05/2018

FRONTLINE VET LABS
A DIVISION OF MERIAL LIMITED

[1] Parasite Prevalence Maps. Companion Animal Parasite Council website. https://www.capcvet.org/maps/#2017/all/lyme-disease/dog/united-states/. Accessed August 15, 2018.

[2] Elevated risk of heartworm disease and Lyme disease continues in 2018. Companion Animal Parasite Council website. https://www.capcvet.org/articles/elevated-risk-of-heartworm-disease-and-lyme-disease-continues-in-2018/. Accessed August 15, 2018.

[3] Freedom of Information Summary, Supplemental NADA 141-406. NexGard (afoxolaner). July 13, 2018.

When Owners Refuse Euthanasia

Euthanasia can become an even more sensitive topic when owners decline to euthanize a patient that is perceived to be suffering. Opposition to euthanasia can arise from an owner's fear of being judged. Normalizing the situation (eg, "Many in your situation would consider euthanasia") or showing support (eg, "I would fully support you in your decision to euthanize") can be helpful. Some owners may be unaware of how ill the pet is; in these cases, emphasizing the gravity of the situation can be helpful.

Personal, cultural, or religious beliefs may be factors in an owner's perception of euthanasia. Open-ended questions can help reveal owner concerns and allow the clinician to explain the euthanasia process, potentially making the owner more receptive to the clinician's point of view. Ultimately, some owners choose natural death over euthanasia. In such situations, palliative care (eg, sedation, opioids [for pain and dyspnea], supplemental oxygen) can be provided. Nebulized furosemide can relieve dyspnea and cough; antiemetics can alleviate nausea. In extreme cases, a medically induced coma or mechanical ventilation can be attempted.

It is paramount that the veterinary team is supported through the euthanasia process. Otherwise, frustration, anger, and compassion fatigue may set in. Including team members in owner communication and in formulating the care plan may alleviate distress and improve empathy.—*Culler CA*

It is paramount that the veterinary team is supported through the euthanasia process.

PRACTICE HOTLINE

The latest in products and services

Boehringer Ingelheim Donates Rabies Vaccines

Merial (**merial.com**), now a part of **Boehringer Ingelheim** (**boehringer-ingelheim.com**), has announced that it will donate 75 000 rabies vaccines to the **Global Alliance for Rabies Control** (**rabiesalliance.org**) in recognition of World Rabies Day on September 28, 2018. The donation is the result of the Shots for Good initiative, through which Boehringer Ingelheim pledged to donate rabies vaccines for every dose of PureVax, Recombitek, and IMRAB vaccine purchased by participating veterinary practices from July 2 to August 10, 2018. The donation will support a mass dog vaccination campaign in Madagascar.—*Press Release 9/2018*

AAHA Releases New Preventive Care Protocols

The **American Animal Hospital Association** (AAHA; **aaha.org**) has released *Promoting Preventive Care Protocols: Evidence, Enactment, and Economics*, a publication developed with the support of an educational grant from **IDEXX** (**idexx.com**). The publication features the results of various studies and concludes that regular health checks and screenings improve disease detection and allow for early therapeutic intervention. A guide is also provided to help veterinary teams implement preventive care protocols, and the value of pet owner communication is highlighted.—*Press Release 9/2018*

2018 Diabetes Pet Care Alliance Program

Merck Animal Health (**merck-animal-health.com**), **Purina** (**purina.com**), and **Zoetis** (**zoetis.com**) have teamed up again to provide free diabetes education and diagnostic tools to veterinarians and pet owners for Pet Diabetes Month in November. Veterinarians who enroll in the **Diabetes Pet Care Alliance** (**usa.petdiabetesmonth.com**) program will gain access to tools and resources related to diabetes awareness and screening. Owners whose pets are diagnosed during the program period will receive a free disease-management kit from participating practices. The kits includes:

- One AlphaTRAK 2 blood glucose monitoring system from Zoetis
- One 6-lb bag of Purina Pro Plan Veterinary Diets DM Dietetic Management Feline Formula for cats or Purina Pro Plan Veterinary Diets EN Gastroenteric Fiber Balance Dry Formula for dogs
- One 10-mL vial of Vetsulin (porcine insulin zinc suspension) from Merck Animal Health

Program enrollment will be open from September 1 through October 31, 2018. To enroll or learn more, visit usa.petdiabetesmonth.com.—*Press Release 9/2018*

Nutramax Laboratories Releases Imuquin

Nutramax Laboratories (**nutramaxlabs.com**) has launched **Imuquin** (**imuquin.com**), an immune health supplement for dogs and puppies. Imuquin contains NMX580, a combination of β-glucan, omega-3 fatty acids, vitamins, and minerals and has been formulated to provide support of normal immune function. Imuquin is available in 2 formulations: Imuquin (for dogs >6 months of age) and Imuquin Puppy (for dogs <6 months of age). Each carton of Imuquin and Imuquin Puppy contains 30 single-serving flavored powder packets that can be added to the dog's diet.—*Press Release 7/2018*

SEND INFORMATION FOR PRACTICE HOTLINE TO editor@cliniciansbrief.com

vetmedin®
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BECAUSE OF VETMEDIN

"I have clients who notice a great response with VETMEDIN. Their animal feels perkier at home, they're brighter, their heart failure is well-controlled, they really feel like themselves. Or they feel like a puppy again, a lot of people say. Which I think is what we all want for our pet."

–Dr Danielle Laughlin
Cardiologist
Blue Pearl Specialty + Emergency Pet Hospital
Sandy Springs, GA

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This testimonial is provided by an actual veterinarian who prescribes VETMEDIN and has been compensated for providing this statement. Individual results may vary. VETMEDIN can only be prescribed by a licensed veterinarian. Please consult a veterinary professional before starting treatment with VETMEDIN.

IMPORTANT SAFETY INFORMATION: Use only in dogs with clinical evidence of heart failure. The most common side effects reported in field studies were poor appetite, lethargy, diarrhea, dyspnea, azotemia, weakness, and ataxia. If side effects should occur, pet owners should contact their veterinarian. The safety of VETMEDIN has not been established in dogs with asymptomatic heart disease or in heart failure caused by etiologies other than atrioventricular valvular insufficiency or dilated cardiomyopathy. VETMEDIN should not be given in case of hypertrophic cardiomyopathy, aortic stenosis, or any other clinical condition where an augmentation of cardiac output is inappropriate for functional or anatomical reasons. The safe use of VETMEDIN has not been evaluated in dogs younger than 6 months of age, dogs with congenital heart defects, dogs with diabetes mellitus or other serious metabolic diseases, dogs used for breeding, or pregnant or lactating bitches. Please refer to the package insert for complete product information or visit **www.vetmedin.com.**

Please see Brief Summary on page 25.

Boehringer Ingelheim

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EXPECT MORE

FROM YOUR GI NUTRITIONAL SOLUTIONS

When it comes to treating GI upset, your go-to solutions may not address specific dietary needs—some patients need a low-fat diet, others need high-calorie formulas. Expect more from your GI solutions with two tailored formulas that offer the same restorative benefits:

HIGH ENERGY DENSITY

Calorically dense to minimize intestinal load and maximize nutrition for pets with poor appetites

LOW FAT

Low fat concentration to help dogs with difficulty digesting fat

BOTH DIETS FEATURE:

- **Zeolite** to absorb excess water and toxins
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- **High digestibility** to ensure optimal nutrient absorption

Get more from your GI solutions. Contact your Royal Canin® representative.

Increased Total Thyroxine

Shanna Hillsman, LVMT
M. Katherine Tolbert, DVM, PhD, DACVIM (SAIM)
University of Tennessee

FOR MORE
Find more Differential Diagnosis lists in upcoming issues of *Clinician's Brief* and on cliniciansbrief.com

- Hypoglycemia
- Epistaxis
- Regurgitation
- Decreased Total Thyroxine

Following are differential diagnoses, listed in order of likeliness, for patients presented with increased total thyroxine.

- Hyperthyroidism
  - Functional benign adenomatous hyperplasia
  - Functional thyroid carcinoma
  - Thyroxine oversupplementation
  - Dietary causes
- Analytical error (eg, false positive)

References

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Peterson ME, Melián C, Nichols R. Measurement of serum concentrations of free thyroxine, total thyroxine, and total triiodothyronine in cats with hyperthyroidism and cats with nonthyroidal disease. *J Am Vet Med Assoc*. 2001;218(4):529-536.

Thompson M. *Small Animal Medical Differential Diagnosis*. St. Louis, MO: Elsevier Saunders; 2007.

Decreased Total Thyroxine

Shanna Hillsman, LVMT
M. Katherine Tolbert, DVM, PhD, DACVIM (SAIM)
University of Tennessee

FOR MORE
Find more Differential Diagnosis lists in upcoming issues of *Clinician's Brief* and on cliniciansbrief.com

- Increased Total Thyroxine
- Hypoglycemia
- Epistaxis
- Regurgitation

Following are differential diagnoses, listed in order of likeliness, for patients presented with decreased total thyroxine.

- Nonthyroidal illness (eg, euthyroid sick syndrome)
- Hypothyroidism
  - Lymphocytic thyroiditis
  - Thyroid atrophy
  - Iatrogenic secondary to radioactive iodine therapy
  - Methimazole therapy
  - Thyroid neoplasia
  - Sulfonamides
  - Congenital
- Hyperadrenocorticism
- Drug effects
  - Phenobarbital
  - Potassium bromide
  - Carprofen
  - Clomipramine
  - Glucocorticoids
  - Propranolol
- Analytical error

References

Peterson ME. Feline focus: diagnostic testing for feline thyroid disease: hypothyroidism. *Compend Contin Educ Vet*. 2013;35(8):E4.

Thompson M. *Small Animal Medical Differential Diagnosis*. St. Louis, MO: Elsevier Saunders; 2007.

Defend against plaque, calculus, and halitosis

Fight the source of oral health problems with the science of delmopinol.

VETERINARY ORAL HEALTH COUNCIL VOHC Accepted® HELPS CONTROL TARTAR

The only chews with the power of delmopinol, **ORAVET®** Dental Hygiene Chews create a barrier against bacterial attachment—and when bacteria can't attach, they can't produce plaque biofilms or the volatile sulfur compounds of halitosis. **ORAVET** Dental Hygiene Chews have been proven effective in multiple canine trials, including "clean mouth" and "dirty mouth" studies.[1,2] They are also highly palatable,[1] and the scrubbing action of the chew works in parallel with delmopinol to remove existing plaque and calculus. For full study results, contact your sales representative or visit **oravet.com.**

*Compared with dogs receiving dry diet alone
References: 1. Data on file. **2.** Data on file.

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DENTAL HYGIENE CHEWS
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GALLIPRANT® (grapiprant tablets)

For oral use in dogs only

20 mg, 60 mg and 100 mg flavored tablets

A prostaglandin E_2 (PGE_2) EP4 receptor antagonist; a non-cyclooxygenase inhibiting, non-steroidal anti-inflammatory drug

Caution: Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.

Before using this product, please consult the product insert, a summary of which follows:

Indication: GALLIPRANT (grapiprant tablets) is indicated for the control of pain and inflammation associated with osteoarthritis in dogs.

Dosage and Administration: Always provide "Information for Dog Owners" Sheet with prescription. Use the lowest effective dose for the shortest duration consistent with individual response.

The dose of GALLIPRANT (grapiprant tablets) is 0.9 mg/lb (2 mg/kg) once daily.

GALLIPRANT tablets are scored and dosage should be calculated in half tablet increments. Dogs less than 8 lbs (3.6 kgs) cannot be accurately dosed. **See product insert for complete dosing and administration information.**

Contraindications: GALLIPRANT should not be used in dogs that have a hypersensitivity to grapiprant.

Warnings: Not for use in humans. Keep this and all medications out of reach of children and pets. Consult a physician in case of accidental ingestion by humans. **For use in dogs only.** Store GALLIPRANT out of reach of dogs and other pets in a secured location in order to prevent accidental ingestion or overdose.

Precautions: The safe use of GALLIPRANT has not been evaluated in dogs younger than 9 months of age and less than 8 lbs (3.6 kg), dogs used for breeding, or in pregnant or lactating dogs. Adverse reactions in dogs receiving GALLIPRANT may include vomiting, diarrhea, decreased appetite, mucoid, watery or bloody stools, and decreases in serum albumin and total protein.

If GALLIPRANT is used long term, appropriate monitoring is recommended.

Concurrent use with other anti-inflammatory drugs has not been studied. Concomitant use of GALLIPRANT with other anti-inflammatory drugs, such as COX-inhibiting NSAIDs or corticosteroids, should be avoided. If additional pain medication is needed after a daily dose of GALLIPRANT, a non-NSAID/non-corticosteroid class of analgesic may be necessary.

The concomitant use of protein-bound drugs with GALLIPRANT has not been studied. Commonly used protein-bound drugs include cardiac, anticonvulsant and behavioral medications.

Drug compatibility should be monitored in patients requiring adjunctive therapy. Consider appropriate washout times when switching from one anti-inflammatory to another or when switching from corticosteroids or COX-inhibiting NSAIDs to GALLIPRANT use.

The use of GALLIPRANT in dogs with cardiac disease has not been studied.

It is not known whether dogs with a history of hypersensitivity to sulfonamide drugs will exhibit hypersensitivity to GALLIPRANT. GALLIPRANT is a methylbenzenesulfonamide.

Adverse Reactions: In a controlled field study, 285 dogs were evaluated for safety when given either GALLIPRANT or a vehicle control (tablet minus galliprant) at a dose of 2 mg/kg (0.9 mg/lb) once daily for 28 days. GALLIPRANT-treated dogs ranged in age from 2 yrs to 16.75 years. The following adverse reactions were observed:

Adverse reaction*	GALLIPRANT (grapiprant tablets) N = 141	Vehicle control (tablets minus grapiprant) N = 144
Vomiting	24	9
Diarrhea, soft stool	17	13
Anorexia, inappetence	9	7
Lethargy	6	2
Buccal ulcer	1	0
Immune mediated hemolytic anemia	1	0

*Dogs may have experienced more than one type or occurrence during the study.

GALLIPRANT was used safely during the field studies with other concurrent therapies, including antibiotics, parasiticides and vaccinations.

To report suspected adverse drug events and/or obtain a copy of the Safety Data Sheet (SDS) or for technical assistance, call 1-888-545-5973.

For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at http://www.fda.gov/AnimalVeterinary/SafetyHealth

Information for Dog Owners: Owners should be advised of the potential for adverse reactions and be informed of the clinical signs associated with drug intolerance. Adverse reactions may include vomiting, diarrhea, decreased appetite, and decreasing albumin and total protein. Appetite and stools should be monitored and owners should be advised to consult with their veterinarian if appetite decreases or stools become abnormal.

Effectiveness: Two hundred and eighty five (285) client-owned dogs were enrolled in the study and evaluated for field safety. GALLIPRANT-treated dogs ranging in age from 2 to 16.75 years and weighing between 4.1 and 59.6 kgs (9-131 lbs) with radiographic and clinical signs of osteoarthritis were enrolled in a placebo-controlled, masked field study. Dogs had a 7-day washout from NSAID or other current OA therapy. Two hundred and sixty two (262) of the 285 dogs were included in the effectiveness evaluation. Dogs were assessed for improvements in pain and function by the owners using the Canine Brief Pain Inventory (CBPI) scoring system.[1] A statistically significant difference in the proportion of treatment successes in the GALLIPRANT group (63/131 or 48.1%) was observed compared to the vehicle control group (41/131 or 31.3%). GALLIPRANT demonstrated statistically significant differences in owner assessed pain and function. The results of the field study demonstrate that GALLIPRANT, administered at 2 mg/kg (0.9 mg/pound) once daily for 28 days was effective for the control of pain and inflammation associated with osteoarthritis.

Storage Conditions: Store at or below 86° F (30° C)

How Supplied: 20 mg, 60 mg, 100 mg flavored tablets in 7, 30 and 90 count bottles.

ARATANA THERAPEUTICS

NADA 141-455, Approved by FDA
US Patents: 6,710,054; 7,960,407; 9,265,756
Made in New Zealand Manufactured for: Aratana Therapeutics, Inc., Leawood, KS 66211
Reference: 1. http://www.vet.upenn.edu/docs/default-source/VCIC/canine-bpi_userguide.pdf?sfvrsn=0
Additional information is available at 1-888-545-5973.
GALLIPRANT is a trademark of Aratana Therapeutics, Inc.

Brief Summary: AT1-040-16

Indication

Galliprant is an NSAID indicated for the control of pain and inflammation associated with osteoarthritis (OA) in dogs.

Important Safety Information

Not for use in humans. For use in dogs only. Keep this and all medications out of reach of children and pets. Store out of reach of dogs and other pets in a secured location in order to prevent accidental ingestion or overdose. Do not use in dogs that have a hypersensitivity to grapiprant. If Galliprant is used long term, appropriate monitoring is recommended. Concomitant use of Galliprant with other anti-inflammatory drugs, such as COX-inhibiting NSAIDs or corticosteroids, should be avoided. Concurrent use with other anti-inflammatory drugs or protein-bound drugs has not been studied. The safe use of Galliprant has not been evaluated in dogs younger than 9 months of age and less than 8 lbs (3.6 kg), dogs used for breeding, pregnant or lactating dogs, or dogs with cardiac disease. The most common adverse reactions were vomiting, diarrhea, decreased appetite, and lethargy. Please see brief summary to the left for full prescribing information.

Galliprant® (grapiprant tablets)

START SEEING CANINE OA FROM A DIFFERENT PERSPECTIVE

Treat OA from the earliest diagnosed stages with Galliprant® (grapiprant tablets), a first-in-class prostaglandin receptor antagonist (PRA) that is a non-COX inhibiting NSAID.

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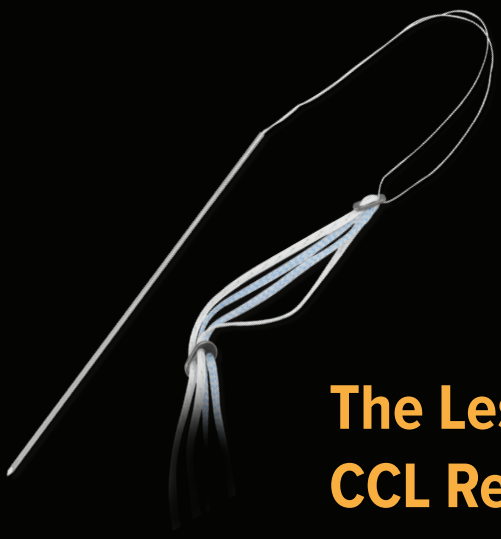

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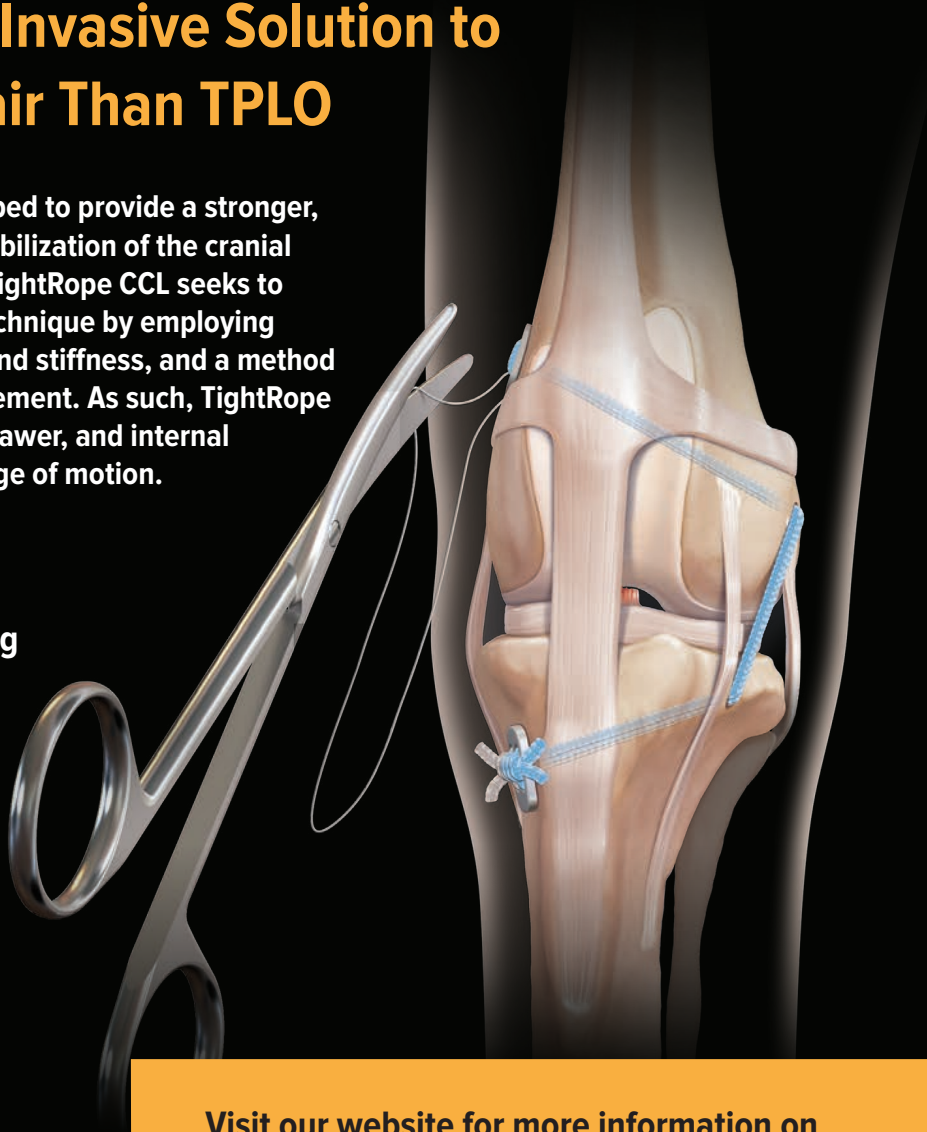
The Less Invasive Solution to CCL Repair Than TPLO

The TightRope CCL technique was developed to provide a stronger, reproducible method for extracapsular stabilization of the cranial cruciate ligament-deficient canine stifle. TightRope CCL seeks to optimize the lateral suture stabilization technique by employing bone-to-bone fixation, superior strength and stiffness, and a method for consistent near isometric implant placement. As such, TightRope CCL can counteract cranial tibial thrust, drawer, and internal rotation, while providing optimal joint range of motion.



TightRope CCL advantages:

- Over 2,500 clinical cases reporting data up to five years out[1]
- 94.4% success rate[2]
- Bone-to-bone fixation

References
1. Data on File
2. Data on File

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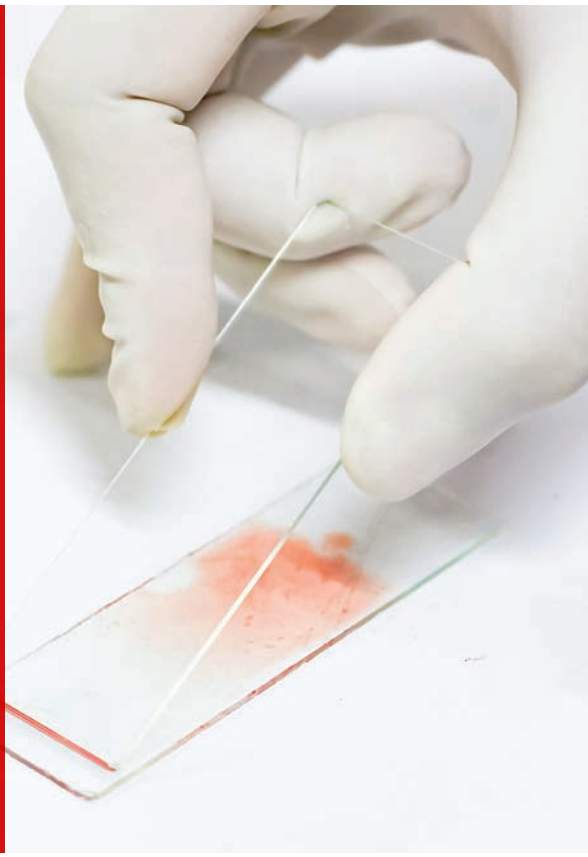
Top 5 Suggestions of Canine Hyperadrenocorticism



Todd Archer, DVM, MS, DACVIM
Mississippi State University

Canine hyperadrenocorticism is a clinical disorder characterized by several common clinical signs, including polyuria, polydipsia, polyphagia, alopecia, thin skin, a pot-bellied appearance, and panting.[1] Hyperadrenocorticism results from excess cortisol production secondary to either an adrenal tumor or a pituitary tumor, causing excessive production of adrenocorticotropic hormone (and, subsequently, an excess production of cortisol).[1]

After a patient has been assessed through a detailed history and physical examination, preliminary testing should be performed prior to specific endocrine testing and should include CBC, serum chemistry profile, and urinalysis. Findings consistent with canine hyperadrenocorticism suggest that further endocrine testing is needed to arrive at a specific diagnosis of canine hyperadrenocorticism.

Following are the author's 5 most common findings seen on CBC, serum chemistry profile, and urinalysis results in patients with confirmed canine hyperadrenocorticism.

1 Stress Leukogram & Thrombocytosis

A stress leukogram is a common but nonspecific finding in dogs with hyperadrenocorticism. It often consists of lymphopenia,

TOP 5 SUGGESTIONS OF CANINE HYPERADRENOCORTICISM

1. Stress Leukogram & Thrombocytosis
2. Elevated Liver Enzymes
3. Hyperglycemia
4. Hypercholesterolemia
5. Dilute Urine

eosinopenia, leukocytosis characterized by mature neutrophilia, and, occasionally, monocytosis.[2] Multiple factors contribute to the development of mature neutrophilia, including an increased release of mature neutrophils from the bone marrow, a shift of marginated neutrophils from the periphery into circulation, and/or a decreased amount of neutrophils leaving the circulation into tissue.[2] Lymphopenia occurs as a result of a redistribution of lymphocytes within the circulation, as well as possible lympholysis.[2] Eosinopenia occurs through steroid-induced sequestration of eosinophils in bone marrow and in other tissues.[2] If monocytosis is present, it is thought to result from a shift of marginated monocytes from the periphery into circulation.[2]

A high-normal–to–increased platelet count may also be found on CBC. As many as 75% to 80% of dogs may have thrombocytosis at the time of diagnosis.[1]

2 Elevated Liver Enzymes

Serum alkaline phosphatase (ALP) and alanine aminotransferase (ALT) are often elevated in dogs with hyperadrenocorticism. ALP tissue activity can be found in the intestine, kidney, liver, and bone.[3] The liver is thought to contribute the majority of ALP measured on serum chemistry profile, with bone being a minor contributor.[1] Little to no intestinal or renal ALP isoenzyme activity has been found in the serum of dogs because of the extremely short half-life.[1] In the liver, the primary location of ALP is the bile canalicular membrane of hepatocytes.[3] In dogs, steroids (exogenous or endogenous) cause an increase in ALP of hepatic origin (ie, the corticosteroid-induced isoenzyme of ALP). This steroid-induced increase in ALP is the most common abnormality found on serum chemistry profile in dogs with hyperadrenocorticism, with incidence at diagnosis often as high as 85% to 95%.[4]

Dogs with hyperadrenocorticism often have mild hyperglycemia (30%-40% of affected patients).[5]

ALT is a cellular leakage enzyme, and elevations are primarily thought to come from hepatocyte injury/damage. ALT also originates from skeletal muscle, and elevated ALT could come from muscle trauma or a myopathy. Measurement of creatinine kinase can help distinguish the source of increased ALT between liver and muscle. In dogs with hyperadrenocorticism, the increase in ALT is thought to occur secondary to hepatocyte damage from swollen hepatocytes, hepatocellular necrosis, accumulation of glycogen, and/or disturbances in hepatic blood flow.[4]

Whereas increases in ALT are typically mild, increases in ALP can range from mild to severe, with severe increases being as high as 10 times the upper limit of the normal reference interval. Liver enzyme elevations vary widely among affected individual dogs.[4]

3 Hyperglycemia

Dogs with hyperadrenocorticism often have mild hyperglycemia (30%-40% of affected patients).[5] The ability of cortisol to increase hepatic gluconeogenesis—as well as its antagonistic effects on insulin in peripheral tissue, which decrease peripheral utilization of glucose—can cause blood glucose to increase.[4] Hypercortisolism-induced hyperinsulinemia may subsequently develop as the pancreas continues to secrete insulin in an attempt to maintain normoglycemia; however, many dogs will have only mild hyperglycemia at diagnosis. A small subset of dogs will have overt

diabetes (glucose, >250 mg/dL [>13.875 mmol/L] with glucosuria and consistent clinical signs) in addition to hyperadrenocorticism.[4] Thus, the elevation in glucose must be critically evaluated to determine if diabetes is present.

4 Hypercholesterolemia

Elevated cholesterol is often noted on serum chemistry profile results in dogs with hyperadrenocorticism. Glucocorticoids can increase lipolysis in adipose tissue, generating both free fatty acids and glycerol, which serve as substrates for gluconeogenesis. This lipolysis in adipose tissue leads to an increase in blood cholesterol. Approximately 90% of dogs with hyperadrenocorticism will have hypercholesterolemia at diagnosis.[1]

5 Dilute Urine

Two of the most common clinical signs associated with canine hyperadrenocorticism are polyuria and polydipsia, which are observed in approximately 90% of patients with hyperadrenocorticism.[4] Although the causes of polyuria and polydipsia can include several factors, polyuria has generally been thought to develop before polydipsia. The influence of cortisol at the level of the kidney causes an impaired tubule response to antidiuretic hormone,[6] which prevents appropriate water reabsorption and causes urine to be less concentrated. Polydipsia subsequently develops to maintain hydration. This is considered a form of secondary nephrogenic diabetes insipidus in which there is a lack of kidney response to antidiuretic hormone. In most dogs, urine specific gravity is less than 1.030[4]; these dogs are also often found to be isosthenuric (ie, having a urine specific gravity of 1.007-1.015).[7]

Conclusion

A minority of patients with hyperadrenocorticism may be presented with polyuria, polydipsia, and dilute urine but have no other clinical abnormalities on CBC, serum chemistry profile, or urinalysis. Lack of a stress leukogram, liver enzyme elevation, hyperglycemia, or hypercholesterolemia should not prevent clinicians from performing specific endocrine testing for canine hyperadrenocorticism. Although most dogs with hyperadrenocorticism will have one or more abnormalities on CBC and serum chemistry profile, the condition should still be included on the differential list in any dog with polyuria and polydipsia, dilute urine, and normal CBC and serum chemistry profile results.

ALP = alkaline phosphatase
ALT = alanine aminotransferase

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Pruritus & Neuropathic Pain in a Dog

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History

A 4-year-old, 55-lb (25-kg), neutered male Portuguese water dog was presented for a 1-year history of intractable pruritus and excessive licking of the lateral aspect of the 5th digit of the left pelvic limb. BCS was 5/9. The pruritus began concomitantly with the growth of an erythematous cutaneous mass localized between the 4th and 5th digit on the same paw, which was later diagnosed as an abscess. The patient received an injectable course of antibiotics and corticosteroids followed by 2 oral antibiotic and corticosteroid courses over a 5-month period. There was no treatment response, so surgical excision of the mass was performed.

After the surgery, pruritus became almost continuous (10/10 using a canine pruritus severity scale[1]) and persisted even after the wound had healed. A second surgical procedure was performed 3 months after the first surgery to debride the wound, and the skin over the 4th and 5th digits was fused. The patient continued to exhibit compulsive licking and biting of the pelvic limb postoperatively, so the owners were instructed to use an Elizabethan collar or a sock over the affected paw to prevent self-mutilation.

Because pruritus persisted, radiography and ultrasonography of the distal limb were performed; no abnormalities were present. Prednisone (0.5 mg/kg PO q24h) and diphenhydramine (2.2 mg/kg PO q8h) were administered, and the degree of pruritus decreased to 3/10. The patient was referred to a dermatologist, who administered amoxicillin–clavulanic acid for treatment of suspected pyoderma. Pruritus was diminished but not resolved (2/10). Localized biting and licking in absence of an obvious local underlying cause was suggestive of a neurologic etiology, and the dog was

referred to a board-certified neurologist for further diagnostic investigation.

Physical Examination

Physical examination was unremarkable except for a 4-cm area of alopecia over the distal and dorsolateral aspect of the left pelvic limb and compulsive licking induced by a light touch and pin prick over the sensory distribution of the tibial nerve from the tibiofemoral joint to the extremity of the limb. The patient's responses to the light touch and pin prick were thought to represent allodynia and hyperalgesia, respectively. Neurologic examination revealed the following changes:

- Stiffness of the left pelvic limb characterized by weak flexion of the stifle and short strides
- The patient favored a resting position in semisternal recumbency (ie, patient lying on his chest and left pelvic limb).
- Decreased postural reactions on the left pelvic limb as compared with the ipsilateral side, which was normal
- Normal spinal reflexes except for an incomplete left pelvic limb withdrawal reflex as compared with the ipsilateral side, which was normal
- Pain elicited (ie, the patient flinched) on palpation of the lumbosacral junction

TREATMENT AT A GLANCE

- Gabapentinoids (eg, gabapentin) to block calcium currents involved in the maintenance of spinal cord central sensitization
- *N*-methyl-D-aspartate antagonists (eg, amantadine, ketamine) to prevent or treat central sensitization
- NSAIDs to reduce peripheral inflammation and hyperalgesia
- Transcutaneous electrical nerve stimulation used as an adjuvant therapy and as part of a multimodal analgesic approach

Diagnosis

CBC and serum chemistry profile results were within normal limits. CT of the left pelvic limb and lumbosacral junction revealed a mild protrusion of the intervertebral disk at the lumbosacral junction, without evidence of compression of the cauda equina or L7 spinal root. Left iliac medial and popliteal lymphadenopathy were reported. MRI of the lumbosacral junction confirmed the protrusion at L7-S1 and showed another protrusive but apparently noncompressive disk at L6-L7. Bone remodeling of the cranial facet of S1 was noted protruding into the vertebral canal. Dynamic impingement could not be ruled out.

Concomitant allodynia and hyperalgesia localized over the area of the tibial nerve were suggestive of neuropathic pain.

DIAGNOSIS:
INTERVERTEBRAL DISK DISEASE

Discussion

In this case, spontaneous pruritus and excessive licking resulting in secondary abscess formation were thought to represent a sign of abnormal sensation in the affected limb (ie, dysesthesia). Neuropathic pain has no physiologic purpose and involves a lesion of the somatosensory system. Concomitant allodynia and hyperalgesia constitute a component of neuropathic pain. According to the International Association for the Study of Pain, *allodynia* refers to pain caused by a stimulus that does not normally provoke pain, whereas *hyperalgesia* corresponds to an increased sensitivity to noxious stimulation.[2] Limb nerve entrapment and lumbosacral lesions have been described as potential causes for neuropathic pain in dogs.[3,4] Diagnosis of neuropathic pain may be challenging due to the lack of validated tools for its assessment.

Treatment & Long-Term Management

The owners declined surgery and opted for medical

management. The patient was successfully treated with gabapentin (10 mg/kg PO q8h), meloxicam (0.1 mg/kg PO q24h), and amantadine (3 mg/kg PO q24h). Pruritus decreased with therapy (2/10). The patient itched occasionally. Gabapentinoids (eg, gabapentin) bind to $\alpha_2\delta$-subunits of voltage-dependent calcium channels and block calcium currents involved in the maintenance of spinal cord central sensitization. Nerve injury causes increased glutamate activity. Glutamate binds to *N*-methyl-D-aspartate receptors, which contribute to spinal central sensitization.[5]

Transcutaneous electrical nerve stimulation—a technique used in physiotherapy to alleviate pain via inhibition of presynaptic transmission in the dorsal horn of the spinal cord and increased release of enkephalins, endorphins, and dynorphins—was used as an adjuvant therapy and as part of this patient's multimodal analgesic approach. Transcutaneous electrical nerve stimulation has been used in humans with neuropathic pain as adjunct therapy.[6,7]

Prognosis & Outcome

After 2 months of treatment, meloxicam was decreased to 0.1 mg/kg q48h and amantadine was decreased to approximately 1-2 mg/kg q48h for 2 weeks, when treatment with both drugs was discontinued. Gabapentin (5 mg/kg PO q8h) was used as maintenance therapy, as the dog was mostly comfortable and only occasionally exhibited shaking of the left pelvic limb. Follow-up consultations every 3 months were suggested.

Take-Home Messages

Neuropathic pain is pain caused by a lesion or disease of the somatosensory system and should be suspected in the presence of central sensitization resulting in allodynia and hyperalgesia.[2] Clinical signs of neuropathic pain are nonspecific and often require multidisciplinary collaboration to reach diagnosis. Surgery, primary neurologic disease, diabetes, and osteoarthritis are potential causes of neuropathic pain. The underlying mechanism of neuropathic pain is not fully understood but likely involves hyperexcitability of afferent neurons, peripheral and central sensitization, and activation of the microglia.[3] Neuropathic pain is commonly refractory to conventional analgesia and requires a multimodal approach.[4]

Clinical signs of neuropathic pain are nonspecific and often require multidisciplinary collaboration to reach diagnosis.

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IMMITICIDE® STERILE POWDER (MELARSOMINE DIHYDROCHLORIDE)
Brief Summary: Before Using IMMITICIDE, please consult the product insert, a summary of which follows.

CAUTION
Federal law restricts this drug to use by or on the order of a licensed veterinarian.

WARNING
IMMITICIDE should be administered by deep intramuscular injection in the lumbar (epaxial) muscles (between L3 - L5) ONLY.
DO NOT USE IN ANY OTHER MUSCLE GROUP. DO NOT USE INTRAVENOUSLY.
Care should be taken to avoid superficial injection or leakage. (See SAFETY).

INDICATIONS
IMMITICIDE Sterile Power is indicated for the treatment of stabilized Class 1, 2, and 3 heartworm disease caused by immature (4 month-old, stage L5) to mature adult infections of Dirofilaria immitis in dogs. See full package insert for Heartworm Disease Classification

CONTRAINDICATIONS
IMMITICIDE is contraindicated in dogs with very severe (Class 4) heartworm disease. Patients in this category have Caval Syndrome (D. immitis present in the venae cavae and right atrium).

WARNINGS
(See boxed Warning). For use in dogs only. Safety for use in breeding animals and lactating or pregnant bitches has not been determined.

HUMAN WARNINGS
Keep this and all medications out of the reach of children. Avoid human exposure. Wash hands thoroughly after use or wear gloves. Potentially irritating to eyes. Rinse eyes with copious amounts of water if exposed. Consult a physician in cases of accidental exposure by any route (dermal, oral, or by injection).

PRECAUTIONS
Dogs with heartworm disease are at risk for post-treatment pulmonary thromboembolism (death of worms which may result in fever, weakness, and coughing). Dogs with severe pulmonary arterial disease have an increased risk and may exhibit more severe signs (dyspnea, hemoptysis, right heart failure and possibly death). Dogs should be restricted from exercise after treatment. Studies indicate that adverse reactions may occur after the second injection in the series even if no problems were encountered with the first injection. All patients should be closely monitored during treatment and for up to 24 hours after the last injection.

Special Considerations for Class 3 dogs: Following stabilization, severely ill (Class 3) dogs should be treated according to the alternate dosing regime in an attempt to decrease post-treatment mortality associated with thromboembolism. Post-treatment mortality due to thromboembolism and/or progression of the underlying disease may occur in 10 to 20% of the Class 3 patients treated with IMMITICIDE. Hospitalization post-treatment and strict exercise restriction are recommended. If the alternate dosing regime is used, expect increased injection site reactions on the side receiving the second injection since the skeletal muscles at the first injection site may not have fully recovered (healed). If persistent swelling is present at 1 month, the second injections may be delayed for several weeks up to 1 month.

Special Considerations for Older Dogs: In clinical field trials, dogs 8 years or older experienced more post-treatment depression/lethargy, anorexia/inappetence, and vomiting than younger dogs.

DOSAGE AND ADMINISTRATION
Care must be taken to administer the proper dose deep into epaxial muscles ONLY (see boxed WARNING). Accurately weigh the dog and calculate the volume to be injected based on the dose of 2.5 mg/kg (1.1 mg/lb). This is equivalent to 0.1 mL/kg (0.045 mL/lb). See full product insert for dosing table. Use a 23 gauge 1 inch needle for dogs equal to or less than 10 kg (22 lb) in weight. Use a 22 gauge 1 ½ inch needle for dogs greater than 10 kg (22 lb). Use alternating sides with each administration and avoid injecting at the same lumbar location.

Disease Classification: It is vital to classify the severity of heartworm disease to apply the appropriate dosage regime for IMMITICIDE. See full product insert for Heartworm Disease Classification criteria.
Class 1 and 2: IMMITICIDE should be given in two intramuscular injections of 2.5mg/kg, 24 hours apart. Four months following treatment, a second treatment series (2.5 mg/kg twice, 24 hours apart) can be elected.
Class 3: Alternate Dosing Regime: Dogs with severe (Class 3) heartworm disease should be stabilized prior to treatment and then dosed intramuscularly in the lumbar (L3 - L5) muscles with a single injection of 2.5 mg/kg then approximately 1 month later with 2.5 mg/kg administered twice, 24 hours apart.

SAFETY
IMMITICIDE has a low margin of safety. A single dose of 7.5 mg/kg (3X the recommended dose) can result in pulmonary inflammation, edema, and death. Symptoms of overdose (2x recommended dose) may include excessive salivation, panting, restlessness, fever, vomiting and diarrhea. These symptoms were seen in the clinical trials and all signs resolved within 24 hours. Symptoms of up to 3x the recommended dose included tremors, lethargy, unsteadiness, restlessness, panting, shallow and labored breathing, pulmonary inflammation, edema, and vomiting which progressed to respiratory distress, collapse, and death. Daily administration of 2X and 3X the recommended dose for 14 days caused renal damage in healthy dogs.

In Case of Overdosage:
BAL in Oil Ampules (Dimercaprol Injection, USP) [Akorn, San Clemente, California, at 1-800-223-9851] is reported in the literature to be an antidote for arsenic toxicity and was shown in one study to reduce the signs of toxicity associated with over-dosage of IMMITICIDE. The efficacy of IMMITICIDE may be reduced with co-administration of BAL.

ADVERSE REACTIONS (SIDE EFFECTS)
In clinical field trials, the most common reactions seen in dogs treated with IMMITICIDE were coughing/gagging, depression/lethargy, anorexia/inappetence, fever, lung congestion, and vomiting. Hypersalivation and panting occurred more rarely, however, these signs may occur within 30 minutes of injection and may be severe. Significant irritation was also observed at the intramuscular injection sites, accompanied by pain, swelling, tenderness, and reluctance to move. Generally, injection site reactions were mild to moderate in severity and recovery occurred in 1 week to 1 month, however, firm nodules can persist indefinitely. Avoid superficial or subcutaneous injection and leakage. Heartworm disease may cause death in dogs with or without treatment, especially in the Class 3 dogs.

Post Approval Experience: There have also been rare reports of paresis and paralysis in dogs following administration of IMMITICIDE.

The information provided here is not comprehensive.
The full FDA-approved product insert is available at http://www.merial.us/SiteCollectionDocuments/Immiticide_PI_8.5x11_version.pdf. Consult your veterinarian for further information. For technical assistance, to request a Safety Data Sheet or to report suspected adverse events, call 1-888-637-4251. For additional information about adverse event reporting for animal drugs, contact FDA at 1-888-FDA-VETS, or http://www.fda.gov/AnimalVeterinary.
NADA 141-042 Marketed by Merial, Inc.

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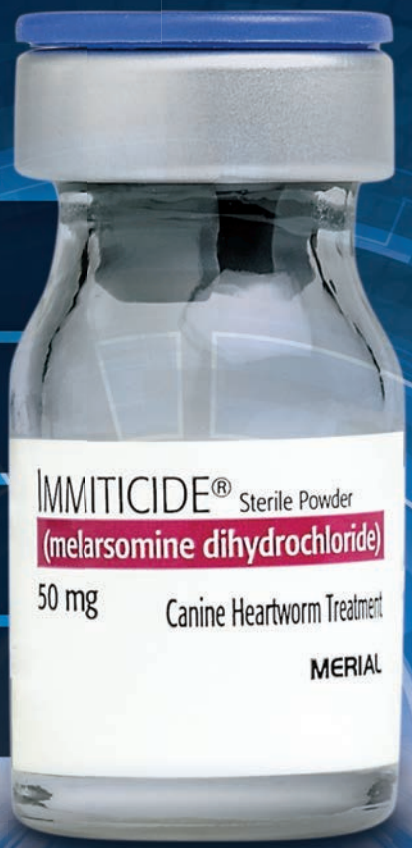

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IMMITICIDE®
(melarsomine dihydrochloride)

IMPORTANT SAFETY INFORMATION: IMMITICIDE should not be used in dogs with very severe (Class 4) heartworm disease. IMMITICIDE should be administered by deep intramuscular injection in the lumbar (epaxial) muscles (L3–L5) only. Do not use in any other muscle group. Do not use intravenously. Care should be taken to avoid superficial injection or leakage. Serious adverse reactions may occur in any dog with heartworm disease due to the killing of heartworms in the pulmonary arteries. Reactions may include thromboembolism, dyspnea, coughing, depression, right side heart failure, and death. Dogs should be cage rested following treatment due to possible thromboembolic disease. Post-injection site reactions (eg. pain, swelling) were the most commonly reported adverse events. See full prescribing information for dosing and administration directions prior to each use of IMMITICIDE.

For more information, please see a summary of the product insert on page 42.

IMMITICIDE is a Merial product. Merial is now part of Boehringer Ingelheim.

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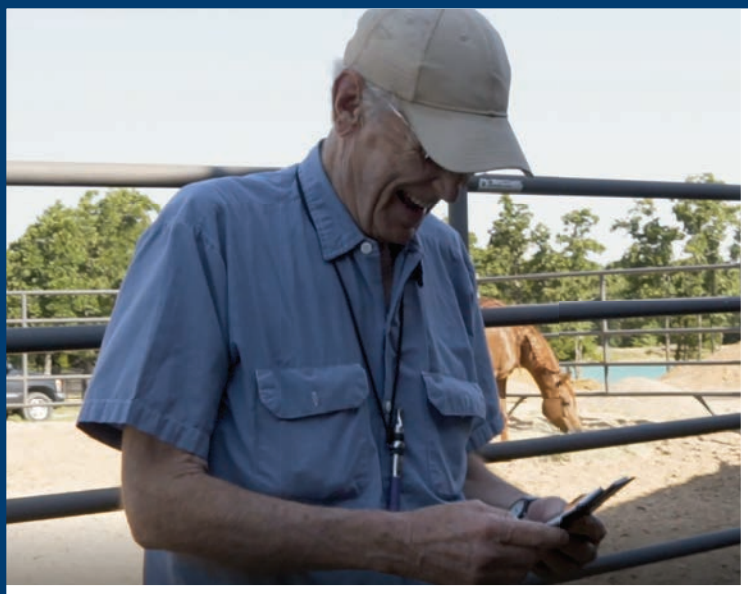

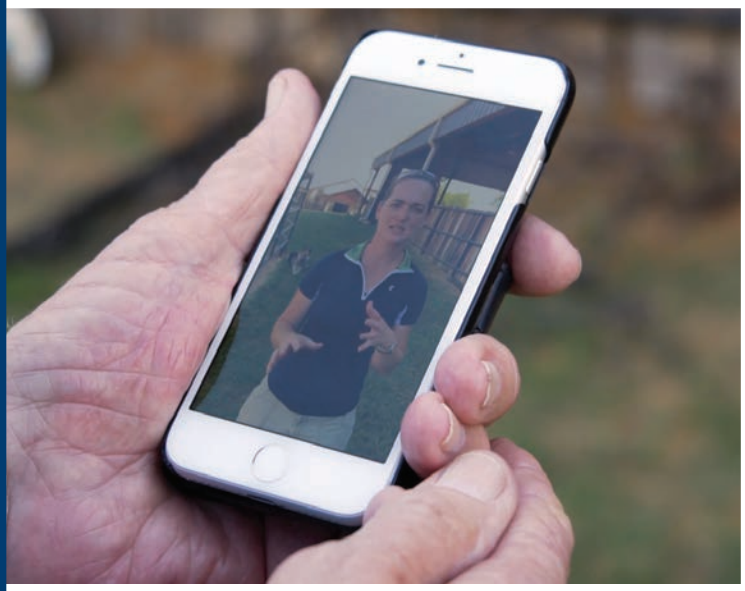

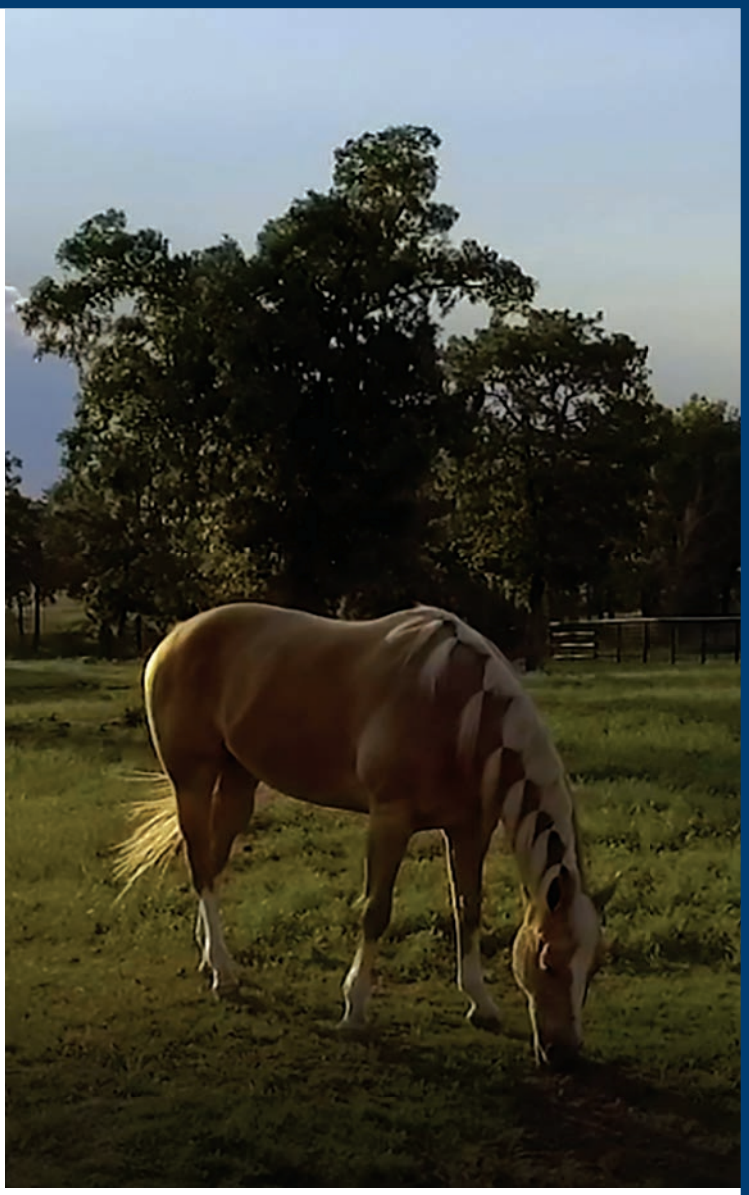

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FROM PAGE TO PATIENT

Designed to bridge the gap between research pages and daily practice protocol, the following pearls offer tips and techniques to grow the general practitioner's clinical excellence.

Lactate in Emergent Dogs & Cats

Selena L. Lane, DVM, DACVECC
University of Georgia

In the Literature

Kohen CJ, Hopper K, Kass PH, Epstein SE. Retrospective evaluation of the prognostic utility of plasma lactate concentration, base deficit, pH, and anion gap in canine and feline emergency patients. *J Vet Emerg Crit Care (San Antonio)*. 2018;28(1):54-61.

FROM THE PAGE ...

Plasma lactate concentration and other acid-base parameters have been associated with patient clinical outcome and provide prognostic information in human ICU and emergency patients. Hyperlactatemia has been shown to provide information on veterinary patient outcomes and is associated with increased illness severity in dogs and cats. It is unknown whether these acid-base derangements are associated with survival in dogs and cats presented to the emergency room.

This retrospective study reviewed records of 566 dogs and 185 cats presented to a university teaching hospital emergency room over a 2-year period. Data collected on each patient included plasma lactate levels, electrolytes, acid-base status, clinical diagnosis, and in-hospital mortality.

Of the study patients, 53% of dogs and 30% of cats had plasma lactate levels >2.5 mmol/L on presentation. Dogs and cats with elevated lactate levels were more likely to have a concurrent metabolic acidosis than to have normal acid-base status. The most common underlying diagnostic categories of dogs with elevated lactate levels were traumatic injury and hemorrhage, neoplasia, and GI disease. In cats, urinary tract disease, traumatic injury and hemorrhage, and GI disease were the most common diagnostic categories associated with hyperlactatemia. Dogs with lactic acidosis had the highest mortality rate (59.8%) of all dogs in the study, which was similar to the high mortality rate (49%) seen in the study cats with lactic acidosis. Cats and dogs with normal blood lactate levels had the lowest mortality rate. Plasma lactate concentration was predictive of mortality in dogs and cats.

These findings are similar to studies performed in humans and support the importance of routine evaluation of lactate and acid-base status in dogs and cats presented on emergency. Evaluation of these parameters can guide owner expectations of outcome in emergent patients and may allow clinicians to recognize patients that may be at highest risk for poor outcome.

... TO YOUR PATIENTS

Key pearls to put into practice:

1. Plasma lactate concentration and acid-base parameters in small animal patients are clinically relevant diagnostic tools and should be used in the emergency room when possible.
2. Lactic acidosis is indicative of more severe underlying disease and should prompt the clinician to monitor patients for decompensation.
3. Lactate concentrations should be measured routinely in emergent patients to provide information about hemodynamic instability and lend insight to patient outcomes.

Suggested Reading

Nye CJ, Musulin SE, Hanel RM, Mariani CL. Evaluation of the Lactate Plus monitor for plasma lactate concentration measurement in dogs. *J Vet Emerg Crit Care (San Antonio)*. 2017;27(1):66-70.

Rosenstein PG, Tennent-Brown BS, Hughes D. Clinical use of plasma lactate concentration. Part 1: physiology, pathophysiology, and measurement. *J Vet Emerg Crit Care (San Antonio)*. 2018;28(2):85-105.

Rosenstein PG, Tennent-Brown BS, Hughes D. Clinical use of plasma lactate concentration. Part 2: prognostic and diagnostic utility and the clinical management of hyperlactatemia. *J Vet Emerg Crit Care (San Antonio)*. 2018;28(2):106-121.

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Oral Melphalan for Refractory Relapsing Canine Lymphoma

Timothy M. Fan, DVM, PhD, DACVIM (Oncology, Internal Medicine)
University of Illinois at Urbana–Champaign

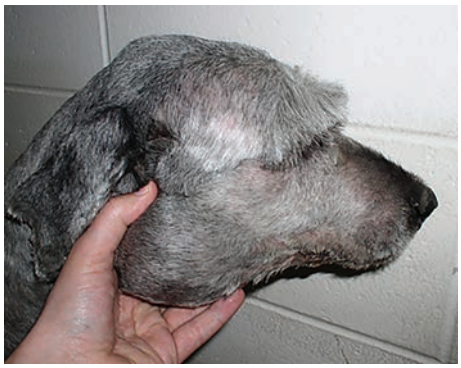
Although melphalan is commonly used for the treatment of multiple myeloma,[5] its activity alone or in combination with prednisone has not been described as a rescue protocol for relapsing lymphoma.

In the Literature

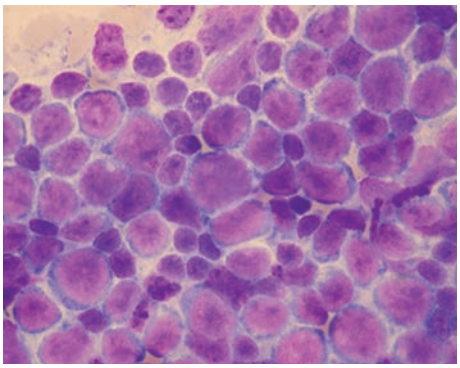
Mastromauro ML, Suter SE, Hauck ML, Hess PR. Oral melphalan for the treatment of relapsed canine lymphoma. *Vet Comp Oncol.* 2018;16(1):E123-E129.

FROM THE PAGE ...

Canine lymphoma has been reported to be responsive to multiagent systemic chemotherapy, with durable and substantive clinical responses (partial and complete remission) achieved in >90% of patients.[1,2] However, most dogs will ultimately experience disease relapse, and subsequent response rates and durations of remission with rescue therapies become progressively lower and shorter, respectively. Use of oral alkylating drugs as rescue agents can be appealing to



▲ **FIGURE 1** Dog with severe mandibular lymphadenopathy associated with relapsing lymphoma



▲ **FIGURE 2** Cytology of aspirated enlarged lymph node confirming a diagnosis of relapsing, diffuse, large-cell lymphoma

pet owners wishing to minimize stress associated with intravenous therapies; however, some alkylating drugs, although modestly effective as rescue drugs, have potential to cause considerable toxicity and reduction of quality of life.[3,4]

This retrospective study examined tolerability and clinical activity of melphalan, an oral alkylating agent, for management of relapsing canine lymphoma. Although melphalan is commonly used for the treatment of multiple myeloma,[5] its activity alone or in combination with prednisone has not been described as a rescue protocol for relapsing lymphoma. In this study, the tolerability and outcomes associated with oral melphalan and prednisone therapy were described in 19 heavily pretreated dogs with relapsing lymphoma. Oral melphalan exerted marginal activity, with an overall calculated clinical benefit of 31.6%. Although anticancer activity was limited, the tolerability profile of oral melphalan was favorable as determined by a low incidence of significant hematologic toxicity and rare GI toxicity.

These findings suggest that oral melphalan alone or in combination with prednisone can reduce lymphoma tumor burden for short durations in some dogs. Given the tolerability of oral melphalan, it might also be considered a palliative option for owners seeking to maintain quality of life without excessive risk for untoward side effects associated with more dose-intense protocols.

… TO YOUR PATIENTS

Key pearls to put into practice:

1. Initial treatment of multicentric lymphoma in dogs is highly effective; however, most dogs will experience disease relapse and require reinstitution of rescue therapies to maintain quality of life and extend survival times.
2. Maintaining quality of life should become centrally important to pet owners of dogs with multicentric lymphoma that have been treated with a multitude of rescue therapies yet experience disease progression.
3. When combined with prednisone therapy, oral melphalan is extremely well tolerated in heavily pretreated dogs and can exert marginal anticancer activities.
4. Given its ease of administration, favorable tolerability, and marginal activity in heavily pretreated dogs with relapsing lymphoma, oral melphalan might be considered a palliative option for pet owners emphasizing quality of life during advanced stages of disease progression.

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Dog Bites in Humans

Audrey Ruple, DVM, MS, PhD, MRCVS, DACVPM
Purdue University

In the Literature

Westgarth C, Brooke M, Christley RM. How many people have been bitten by dogs? A cross-sectional survey of prevalence, incidence and factors associated with dog bites in a UK community. *J Epidemiol Community Health*. 2018;72:331-336.

FROM THE PAGE …

A comprehensive understanding of how often humans are bitten by dogs is lacking, as most research into this topic has been based on hospital-admission records. Although not all dog bites are severe enough to warrant hospitalization, even minor dog bites can impact physical and psychologic health and can therefore be a burden on public health.

The authors of this study recognized the limitations of hospital-based data and aimed to survey the population of a semirural town in northwest England. Of the 694 participants representing 30.1% of households in the town, almost one quarter (24.78%) reported having been bitten by a dog at least once. Medical treatment was required in 33.1% of cases; only one bite resulted in hospitalization.

The authors further investigated human-related factors associated with dog bites and the relationships between humans and the dogs that bit them. It was determined that men were more likely than women to be bitten, and dog owners were

more likely to be bitten than were non-dog owners, with further increased risk to owners of more than one dog. Personality indicators such as insecurity, fear, and instability were also associated with an increased risk for being bitten. More than half of the surveyed respondents were bitten by a dog they had never met before.

It is important to note that this survey was conducted in a limited geographic region and that these results may not be generalizable to a wider population. However, this study does provide the first investigation of dog bite incidence and risk factors at the community level rather than through hospital-admission records. The increased frequency of dog bites reported combined with the low proportion of bites requiring hospital admission lend credibility to the hypothesis that dog bites occur more commonly than reported.

… TO YOUR PATIENTS

Key pearls to put into practice:

1. Pet owners should be informed that although severe dog bites occur relatively infrequently, less severe bites may occur fairly commonly.
2. Owners should be educated about the risk for dog bites from unknown dogs, as owners may be likely to come in contact with unknown dogs while participating in activities with their dog or in public spaces frequented by other dogs (eg, dog parks).
3. Owners with multiple dogs in the household should be informed about the increased risk for being bitten, as owners of multiple dogs may be up to 27 times more likely to be bitten than non-dog owners.

See page 50 for product information summary.

NADA 141-297, Approved by FDA

ProZinc®

(protamine zinc recombinant human insulin)

Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

Description: ProZinc® insulin is a sterile aqueous protamine zinc suspension of recombinant human insulin.

Each mL contains:

recombinant human insulin	40 International Units (IU)
protamine sulfate	0.466 mg
zinc oxide	0.088 mg
glycerin	16.00 mg
dibasic sodium phosphate, heptahydrate	3.78 mg
phenol (added as preservative)	2.50 mg
hydrochloric acid	1.63 mg
water for injection (maximum)	1005 mg

pH is adjusted with hydrochloric acid and/or sodium hydroxide.

Indication: ProZinc (protamine zinc recombinant human insulin) is indicated for the reduction of hyperglycemia and hyperglycemia-associated clinical signs in cats with diabetes mellitus.

Dosage and Administration: USE OF A SYRINGE OTHER THAN A U-40 SYRINGE WILL RESULT IN INCORRECT DOSING.

FOR SUBCUTANEOUS INJECTION IN CATS ONLY.

DO NOT SHAKE OR AGITATE THE VIAL.

ProZinc insulin should be mixed by gently rolling the vial prior to withdrawing each dose from the vial. Once mixed, ProZinc suspension has a white, cloudy appearance. Clumps or visible white particles can form in insulin suspensions: do not use the product if clumps or visible white particles persist after gently rolling the vial. Using a U-40 insulin syringe, the injection should be administered subcutaneously on the back of the neck or on the side of the cat.

Always provide the Cat Owner Information Sheet with each prescription.

The initial recommended ProZinc dose is 0.1 – 0.3 IU insulin/pound of body weight (0.2 – 0.7 IU/kg) every 12 hours. The dose should be given concurrently with or right after a meal. The veterinarian should re-evaluate the cat at appropriate intervals and adjust the dose based on both clinical signs and glucose nadirs until adequate glycemic control has been attained. In the effectiveness field study, glycemic control was considered adequate if the glucose nadir from a 9-hour blood glucose curve was between 80 and 150 mg/dL and clinical signs of hyperglycemia such as polyuria, polydipsia, and weight loss were improved.

Further adjustments in the dosage may be necessary with changes in the cat's diet, body weight, or concomitant medication, or if the cat develops concurrent infection, inflammation, neoplasia, or an additional endocrine or other medical disorder.

Contraindications: ProZinc insulin is contraindicated in cats sensitive to protamine zinc recombinant human insulin or any other ingredients in the ProZinc product. ProZinc insulin is contraindicated during episodes of hypoglycemia.

Warnings: User Safety: For use in cats only. Keep out of the reach of children. Avoid contact with eyes. In case of contact, immediately flush eyes with running water for at least 15 minutes. Accidental injection may cause hypoglycemia. In case of accidental injection, seek medical attention immediately. Exposure to product may induce a local or systemic allergic reaction in sensitized individuals.

Animal Safety: Owners should be advised to observe for signs of hypoglycemia (see Cat Owner Information Sheet). Use of this product, even at established doses, has been associated with hypoglycemia. An animal with signs of hypoglycemia should be treated immediately. Glucose should be given orally or intravenously as dictated by clinical signs. Insulin should be temporarily withheld and, if indicated, the dosage adjusted.

Any change in insulin should be made cautiously and only under a veterinarian's supervision. Changes in insulin strength, manufacturer, type, species (human, animal) or method of manufacture (rDNA versus animal-source insulin) may result in the need for a change in dosage.

Appropriate diagnostic tests should be performed to rule out other endocrinopathies in diabetic cats that are difficult to regulate.

Precautions: Animals presenting with severe ketoacidosis, anorexia, lethargy, and/or vomiting should be stabilized with short-acting insulin and appropriate supportive therapy until their condition is stabilized. As with all insulin products, careful patient monitoring for hypoglycemia and hyperglycemia is essential to attain and maintain adequate glycemic control and to prevent associated complications. Overdosage can result in profound hypoglycemia and death. Progestogens, certain endocrinopathies and glucocorticoids can have an antagonistic effect on insulin activity. Progestogen and glucocorticoid use should be avoided.

Reproductive Safety: The safety and effectiveness of ProZinc insulin in breeding, pregnant, and lactating cats has not been evaluated.

Use in Kittens: The safety and effectiveness of ProZinc insulin in kittens has not been evaluated.

Adverse Reactions:

Effectiveness Field Study

In a 45-day effectiveness field study, 176 cats received ProZinc insulin. Hypoglycemia (defined as a blood glucose value of <50 mg/dL) occurred in 71 of the cats at various times throughout the study. Clinical signs of hypoglycemia were generally mild in nature (described as lethargic, sluggish, weak, trembling, uncoordinated, groggy, glassy-eyed or dazed). In 17 cases, the veterinarian provided oral glucose supplementation or food as treatment. Most cases were not associated with clinical signs and received no treatment. One cat had a serious hypoglycemic event associated with stupor, lateral recumbency, hypothermia and seizures. All cases of hypoglycemia resolved with appropriate therapy and, if needed, a dose reduction.

Three cats had injection site reactions, which were described as either small, punctate, red lesions; lesions on neck; or palpable subcutaneous thickening. All injection site reactions resolved without cessation of therapy.

Four cats developed diabetic neuropathy during the study as evidenced by plantigrade stance. Three cats entered the study with plantigrade stance, one of which resolved by Day 45. Four cats were diagnosed with diabetic ketoacidosis during the study. Two were euthanized due to poor response to treatment. Five other cats were euthanized during the study, one of which had hypoglycemia. Four cats had received ProZinc insulin for less than a week and were euthanized due to worsening concurrent medical conditions.

The following additional clinical observations or diagnoses were reported in cats during the effectiveness field study: vomiting, lethargy, diarrhea, cystitis/hematuria, upper respiratory infection, dry coat, hair loss, ocular discharge, abnormal vocalization, black stool, and rapid breathing.

Extended Use Field Study

Cats that completed the effectiveness study were enrolled into an extended use field study. In this study, 145 cats received ProZinc insulin for up to an additional 136 days. Adverse reactions were similar to those reported during the 45-day effectiveness study and are listed in order of decreasing frequency: vomiting, hypoglycemia, anorexia/poor appetite, diarrhea, lethargy, cystitis/hematuria, and weakness. Twenty cats had signs consistent with hypoglycemia described as: sluggish, lethargic, unsteady, wobbly, seizures, trembling, or dazed. Most of these were treated by the owner or veterinarian with oral glucose supplementation or food; others received intravenous glucose. One cat had a serious hypoglycemic event associated with seizures and blindness. The cat fully recovered after supportive therapy and finished the study. All cases of hypoglycemia resolved with appropriate therapy and if needed, a dose reduction.

Fourteen cats died or were euthanized during the extended use study. In two cases, continued use of insulin despite anorexia and signs of hypoglycemia contributed to the deaths. In one case, the owner decided not to continue therapy after a presumed episode of hypoglycemia. The rest were due to concurrent medical conditions or worsening of the diabetes mellitus.

To report suspected adverse reactions, or to obtain a copy of the Material Safety Data Sheet (MSDS), call 1-866-638-2226.

Information for Cat Owners: Please refer to the Cat Owner Information Sheet for more information about ProZinc insulin. ProZinc insulin, like other insulin products, is not free from adverse reactions. Owners should be advised of the potential for adverse reactions and be informed of the associated clinical signs. Potential adverse reactions include: hypoglycemia, insulin antagonism/resistance, rapid insulin metabolism, insulin-induced hyperglycemia (Somogyi Effect), and local or systemic reactions. The most common adverse reaction observed is hypoglycemia. Signs may include: weakness, depression, behavioral changes, muscle twitching, and anxiety. In severe cases of hypoglycemia, seizures and coma can occur. Hypoglycemia can be fatal if an affected cat does not receive prompt treatment. Appropriate veterinary monitoring of blood glucose, adjustment of insulin dose and regimen as needed, and stabilization of diet and activity help minimize the risk of hypoglycemic episodes. The attending veterinarian should evaluate other adverse reactions on a case-by-case basis to determine if an adjustment in therapy is appropriate, or if alternative therapy should be considered.

Effectiveness: A total of 187 client-owned cats were enrolled in a 45-day field study, with 176 receiving ProZinc insulin. One hundred and fifty-one cats were included in the effectiveness analysis. The patients included various purebred and mixed breed cats ranging in age from 3 to 19 years and in weight from 4.6 to 20.8 pounds. Of the cats included in the effectiveness analysis, 101 were castrated males, 49 were spayed females, and 1 was an intact female.

Cats were started on ProZinc insulin at a dose of 0.1-0.3 IU/lb (0.2-0.7 IU/kg) twice daily. Cats were evaluated at 7, 14, 30, and 45 days after initiation of therapy, and the dose was adjusted based on clinical signs and results of 9-hour blood glucose curves on Days 7, 14, and 30.

Effectiveness was based on successful control of diabetes, which was defined as improvement in at least one blood glucose variable (glucose curve mean, nadir, or fructosamine) and at least one clinical sign (polyuria, polydipsia, or body weight). Based on this definition, 115 of 151 cases (76.2%) were considered successful. Blood glucose curve means decreased from 415.3 mg/dL on Day 0 to 203.2 mg/dL by Day 45, and the mean blood glucose nadir decreased from 407.9 mg/dL on Day 0 to 142.4 mg/dL on Day 45. Mean fructosamine values decreased from 505.9 µmol/L on Day 0 to 380.7 µmol/L on Day 45.

Cats that completed the effectiveness study were enrolled in an extended use field study. The mean fructosamine value was 342.0 µmol/L after a total of 181 days of ProZinc therapy.

How Supplied: ProZinc insulin is supplied as a sterile injectable suspension in 10-mL multidose vials. Each mL of ProZinc product contains 40 IU recombinant human insulin.

Storage Conditions: Store in an upright position under refrigeration at 36-46°F (2-8°C). Do not freeze. Protect from light.

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Important Safety Information: For use in cats only. Animals presenting with severe ketoacidosis, anorexia, lethargy, and/or vomiting should be stabilized with short-acting insulin and appropriate supportive therapy until their condition is stabilized. As with all insulin products, careful patient monitoring for hypoglycemia and hyperglycemia is essential to attain and maintain adequate glycemic control and to prevent associated complications. Overdosage can result in profound hypoglycemia and death. Progestogen and glucocorticoid use should be avoided. PROZINC insulin is contraindicated in cats during episodes of hypoglycemia and in cats sensitive to protamine zinc recombinant human insulin or any other ingredients in the PROZINC product.

References: 1. Nelson RW, Henley K, Cole C; PZIR Clinical Study Group. Field safety and efficacy of protamine zinc recombinant human insulin for treatment of diabetes mellitus in cats. *J Vet Intern Med*. 2009;23(4):787–793. **2.** Nelson RW. Disorders of the endocrine pancreas. In: Nelson RW, Cuoto CG, eds. *Small Animal Internal Medicine*. 4th ed. St. Louis, MO: Mosby Elsevier; 2008:764–802. **3.** Rucinsky R, Cook A, Haley S, Nelson R, Zoran DL, Poundstone M; American Animal Hospital Association (AAHA). AAHA diabetes management guidelines for dogs and cats. *J Am Anim Hosp Assoc*. 2010;46(3):215–224.

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See page 52 for product information summary.

Central Venous Jugular Catheters

Jennifer Good, DVM, DACVECC
University of Georgia Veterinary Teaching Hospital

In the Literature

Reminga CL, Silverstein DC, Drobatz KJ, Clarke DL. Evaluation of the placement and maintenance of central venous jugular catheters in critically ill dogs and cats. *J Vet Emerg Crit Care (San Antonio)*. 2018;28(3):232-243.

FROM THE PAGE ...

Placement of central venous jugular catheters (CVJCs), which use the over-the-wire modified Seldinger technique, can be labor-intensive.[1] CVJCs require sterile placement, daily cleaning and disinfecting, and radiography to confirm proper placement. Benefits of CVJCs include the ability to leave the catheters safely in place for several days, easier blood sampling, and the ability to deliver multiple fluid types or medications, including difficult-to-administer infusions (eg, high-percent dextrose). Catheters range from single to triple lumen and may be placed in a pelvic limb vessel if the length is sufficient to place the catheter tip into the caudal vena cava.

This prospective study of 27 dogs and 20 cats in a veterinary intensive care unit aimed to describe problems noted during CVJC placement, conditions associated with unsuccessful catheterization, and complications of CVJC maintenance. Daily assessment, inspection, and cleansing (with dilute chlorhexidine solution) of the insertion site were performed. The overall success rate for catheter placement was 91.5%, with most catheters successfully placed on the first attempt. Older patients and those with low BCS or weight were more likely to require more than one attempt. No complications were associated with catheter use in 67.4% of patients. Most complications were mechanical obstructions (eg, venous thrombosis, kinking, malposition) and irritation (eg, skin redness, local bruising, bandage-related cervical swelling). Inflammatory complications (eg, sterile phlebitis, catheter-related infections) were the least common. The majority of complications were minor and did not necessitate catheter removal. Level of staff experience and occupation of catheter placer (eg, veterinarian vs veterinary nurse) were not found to affect the number of complications.

... TO YOUR PATIENTS

Key pearls to put into practice:

1. It is worthwhile to become trained in proper CVJC placement to prepare for patients hospitalized for prolonged periods. Use of multilumen catheters can help decrease the number of peripheral blood sticks and overall number of catheters needed.
2. Sterile placement of single-lumen intracatheters can be used in lieu of CVJCs. Single-lumen intracatheters are more common in general practice, come in a variety of lengths, do not require use of the modified Seldinger technique for placement, and can be placed in jugular veins or pelvic limb vessels to allow for repeated blood sampling and IV infusions.
3. Daily unwrapping and cleansing of any catheter sites—peripheral or central—along with the use of gloves and hand-washing between patients can decrease catheter-related infections and should be an important part of hospital protocol.[2]

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Read more about central venous catheter placement with the modified Seldinger technique at **cliniciansbrief.com/modified-seldinger-technique**

Research Note:
Rabies-Neutralizing Antibodies & Rabies Titers

This study retrospectively reviewed serologic data for rabies-neutralizing antibodies in 662 young dogs to evaluate whether certain variables (eg, signalment, number of vaccinations, vaccine brand and multivalence, time interval between the most recent vaccination and blood sampling) affected dogs' ability to achieve acceptable rabies titers. Dogs that had been vaccinated twice before 12 months of age were found to have significantly higher antibody titers than those vaccinated once; those vaccinated with monovalent vaccines were more likely to achieve an acceptable titer than those vaccinated with polyvalent vaccines. Dogs vaccinated after 3 to 6 months of age had higher antibody titers than those vaccinated earlier.

Dogs vaccinated after 3 to 6 months of age had higher antibody titers than those vaccinated earlier.

Source

Tasioudi KE, Papatheodorou D, Iliadou P, et al. Factors influencing the outcome of primary immunization against rabies in young dogs. *Vet Microbiol*. 2018;213:1-4.

Maladaptive Pain in Cats

Tamara Grubb, DVM, PhD, DACVAA
International Veterinary Academy of Pain Management

In the Literature

Adrian D, Papich M, Baynes R, Murrell J, Lascelles BDX. Chronic maladaptive pain in cats: a review of current and future drug treatment options. *Vet J*. 2017;230:52-61.

Aside from NSAIDs, few drugs have been proven to be effective in cats—or other veterinary species—for the treatment of chronic or maladaptive pain.

FROM THE PAGE …

Chronic pain should not be characterized by duration of pain but instead by changes that occur in the nociceptive components of the CNS in response to ongoing stimuli.[1] These changes can lead to maladaptive pain, which has no protective purpose and can lead to a debilitating pain syndrome that is difficult to treat; this contrasts with acute pain, which protects the patient from further tissue damage by promoting limited movement of injured tissue.[1] Although maladaptive pain is likely to occur in cats,[2] there are few proven treatment options.

This review provides a comprehensive discussion of published literature on maladaptive pain and its treatment in cats, with supporting information from other species, including a clear and detailed explanation (with illustrations) of maladaptive pain and the importance of understanding that the disease and its treatment are multifactorial. The importance of pain assessment is discussed, as are potential therapies.

Aside from NSAIDs, few drugs have been proven to be effective in cats—or other veterinary species—for the treatment of chronic or maladaptive pain, and even those proven in humans are not always effective, primarily because of the complexity of the disease. In addition, the common use of acute pain models to test drugs for chronic pain therapy can skew interpretation of a drug's utility.[3,4]

Because of the preservation of the mammalian pain pathway components across species,[5] it is not considered to be anthropomorphization or malpractice to use drugs with proven efficacy in other mammalian species. However, adverse effects may not be the same across species, and safety studies are often more critical than are efficacy studies. Use of this evidence-based review in combination with treatment protocols from pain management experts[6-9] to provide feline patients with evidence-guided pain relief may be beneficial.

… TO YOUR PATIENTS

Key pearls to put into practice:

1. Feline chronic pain should be treated early, and multimodal analgesia should be used, as chronic pain is often actually maladaptive pain, which can be complicated to treat.
2. When designing treatment protocols, clinicians should use evidence-based medicine while also embracing experience-based treatment recommendations from experts.
3. Assessment tools for owners to evaluate pets at home should be recommended. For example, having owners videotape their cat at home before and after treatment and sending the videos to the veterinarian to evaluate may be helpful. Clinicians should be cautious of placebo effects[10] but also understand the ability of owners to detect quality-of-life changes in their pet.[11]

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[1]*Dirofilaria immitis* [2]*Ancylostoma caninum* [3]*Ancylostoma caninum, Uncinaria stenocephala, Ancylostoma braziliense* [4]*Toxocara canis, Toxascaris leonina* [5]*Trichuris vulpis* [6]*Taenia pisiformis, Echinococcus multilocularis, Echinococcus granulosus, Dipylidium caninum*

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Publication title: *Clinician's Brief* **Publication number:** 1542-4014 **Filing date:** 10/1/18 **Issue frequency:** Monthly **Number of issues published annually:** 12 **Annual subscription price:** $55 **Complete mailing address of known office of publication:** 2021 S Lewis Ave, Suite 760, Tulsa, OK 74104 **Contact person:** Natalie Williams **Telephone:** 918-710-4631 **Full name and complete mailing address of Publisher, Editor, & Managing Editor:** Elizabeth Green, 2021 S Lewis Ave, Suite 760, Tulsa, OK 74104; Indu Mani, 2021 S Lewis Ave, Suite 760, Tulsa, OK 74104; Samantha Farley, 2021 S Lewis Ave, Suite 760, Tulsa, OK 74104 **Owner:** Educational Concepts LLC, 2021 S Lewis Ave, Suite 760, Tulsa, OK 74104—Owners: Siegfried Ventures, 1924 S Utica Ave, Tulsa, OK 74104; Elizabeth Green, 2021 S Lewis Ave, Suite 760, Tulsa, OK 74104; John O'Brien, 12118 Nieman Rd, Overland Park, KS 66213; Antoinette Passaretti, 3936 Sawmill Rd, Doylestown, PA 18902 **Known bondholders, mortgages and other security holders owning or holding 1 percent or more of total amount of bonds, mortgages or other securities:** None **Issue date for circulation data below:** September 2018

EXTENT AND NATURE OF CIRCULATION

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CONSULT THE EXPERT PAGE 71

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CASE IN POINT PAGE 39

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CASE IN POINT PAGE 39

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DIFFERENTIAL DIAGNOSIS PAGE 29

DIFFERENTIAL DIAGNOSIS PAGE 30

PROCEDURES PRO

INTERCOSTAL BLOCKS FOR RIB FRACTURES

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Local analgesic techniques—including intercostal, epidural, and spinal blocks—are frequently used to treat pain related to thoracic surgery or trauma (eg, rib fractures).[1]

Pain associated with thoracic trauma, whether surgically induced or traumatic in origin, can lead to hypoventilation, delayed recovery, increased morbidity, and prolonged hospitalization.[1,2] Local anesthesia at the level of the intercostal spaces provides benefits over thoracic epidural anesthesia by inducing less sympathetic blockade, addressing pain closer to the initiation of the pain pathway, and providing complete blockade of all pain fibers, with minimal effect on ventilation.[3] Intercostal nerve blocks have been shown to improve pulmonary function in the postoperative period in human and veterinary patients undergoing thoracotomy[4-6]; in addition, in humans, intercostal nerve blocks used to treat multiple rib fractures have been shown to be effective and to decrease the amount of systemic opioid needed to control pain.[5] Dogs and cats with multiple rib fractures are at risk for decreased pulmonary function and may require high rates of systemic analgesics to control pain.[7]

Relevant Anatomy

The paravertebral space involves the spinal nerve root, which is continuous with the intercostal nerve. This space is not completely segregated; drugs injected into one specific paravertebral space have the potential to spread cranially and caudally into additional paravertebral spaces, as well as medially and laterally into the epidural and intercostal spaces. The intercostal space is continuous

TABLE

LOCAL PERINEURAL ANESTHETIC DOSAGES[1-3]

Drug (Concentration)*	Duration of Action**	Dose (Dogs)	Maximum Dose (Dogs)	Dose (Cats)	Maximum Dose (Cats)
Bupivacaine (0.5% or 0.25%)	4-12 hr (average, ≈6-8 hr)	0.5-1 mg/kg	2 mg/kg	0.25-0.50 mg/kg	1 mg/kg
Lidocaine (2%)	1-2 hr (average, ≈90 min)	1-2 mg/kg	5-6 mg/kg	0.5-1 mg/kg Note: Systemic uptake should be avoided by ensuring the block does not go intravenously	1-2 mg/kg
Morphine (10 mg/mL or 25 mg/mL)	4-6 hr	0.1 mg/kg		0.1 mg/kg	
Methadone (10 mg/mL)	4-6 hr	0.1 mg/kg		0.1 mg/kg	
Dexmedetomidine (0.5 mg/mL)	4-6 hr	1-2 µg/kg		1-2 µg/kg	

* Onset of local analgesia can take up to 20 minutes but depends on the drug(s) used. Rapid-onset drugs (eg, lidocaine, α_2 agonists) can be added to those with slower onset (eg, bupivacaine, opioids) to facilitate a faster onset of analgesia.
** The duration of the block itself is altered by the agents and dose selected for each patient.

with the paravertebral space and involves the nerve roots that branch from the paravertebral nerve and supply the ribs, intercostal muscles, and skin. In general, the neurovascular structures that line the thoracic cavity have both cranial and caudal branches, which divide and supply the skin and intercostal muscles of segments adjacent to that paravertebral space.

Due to this collateral circulation/innervation, blocking sites adjacent to rib fractures is recommended to ensure appropriate analgesia to the intended site. Risks associated with this procedure include iatrogenic pneumothorax, intraneural or intravascular injection, systemic toxicity of local anesthetics, and, rarely, introduction of bacteria into the intercostal or paravertebral space.

Agents for Intercostal Blocks

Drugs used in intercostal blocks can include local anesthetics, opioids, or α_2 agonists; a combination of drugs is often recommended to increase effects on the pain pathway.[1,2,5,8] Bupivacaine, a local anesthetic that provides long-term pain relief, is often recommended because it provides 6 to 8 hours of blockade.[9] Mixing bupivacaine with either an opioid (eg, preservative-free morphine) or an α_2 agonist (eg, dexmedetomidine) can provide additional analgesia by activating local opioid and α_2 receptors and through systemic absorption.[10] A study in humans noted that the risk for local anesthetic toxicity is highest when local anesthetics are administered at the paravertebral space, and another noted that local anesthetics are also rapidly absorbed from the intercostal space.[9]

Care should be taken when calculating drug dosages (***Table***), and the effects of systemic absorption of local anesthetics and adjunctive agents should be considered.[9] If there are multiple rib fracture sites and more volume is needed to appropriately block all ribs, decreasing the dose of bupivacaine and adding lidocaine to increase the volume is ideal; however, this will decrease the overall duration of action. Adding sterile water (or saline) to the volume of local anesthetic may also be appropriate. After the number of fractured ribs is determined, the number of sites to block and the number of aliquots of local anesthetic to prepare should be calculated (see ***Calculating Intercostal Sites***). If multiple ribs are broken on one side, many of these sites will overlap cranially and caudally.

CALCULATING INTERCOSTAL SITES

Fracture Site (rib #) = 7
Cranial Intercostal Spaces: 5-6, 6-7
Affected Space: 7-8
Caudal Intercostal Spaces: 8-9, 9-10
Total Spaces to Block: 5

Fracture Site (rib #) = 4, 6
Cranial Intercostal Spaces: 2-3, 3-4; 4-5, 5-6
Affected Spaces: 4-5, 6-7
Caudal Intercostal Spaces: 5-6, 6-7; 7-8, 8-9
Total Spaces to Block: 8 (Note: Several of these spaces overlap between the 2 fracture sites.)

Blocking sites adjacent to rib fractures is recommended to ensure appropriate analgesia to the intended site.

WHAT YOU WILL NEED

- Clippers and preparation supplies (eg, chlorhexidine scrub, alcohol)
- Gloves
- Selected drugs divided into aliquots based on number of sites to block (see ***Calculating Intercostal Sites***, previous page)
- Aliquots of sterile saline
- New spinal or hypodermic needle (22-25 g) for each site

STEP-BY-STEP INTERCOSTAL BLOCKS FOR RIB FRACTURES

STEP 1

Sedate (or anesthetize, if needed) the patient using an opioid and either a benzodiazepine or an α_2 agonist, depending on the patient's overall cardiovascular and systemic health status.[11]

Author Insight

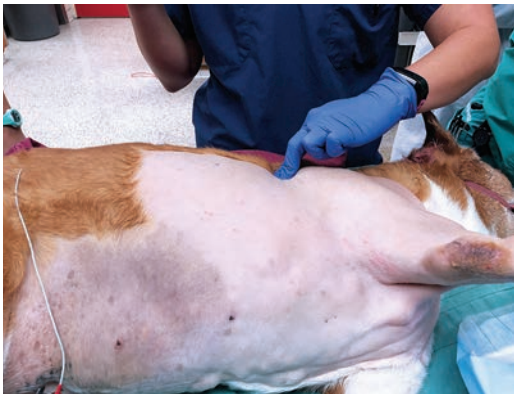
If the patient has suffered fractures due to trauma, electrocardiography and close monitoring should be instituted to observe for evidence of cardiac contusions in the form of arrhythmias. The presence of arrhythmias may change the drug choice for sedation, general anesthesia, and/or paravertebral local blocks.

STEP 2

Obtain thoracic radiographs to confirm the location of the broken rib(s).

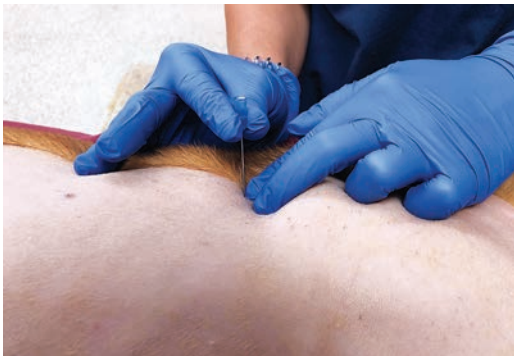
STEP 3

Block at least 2 intercostal spaces cranial to and caudal to the fracture on the ipsilateral side to deliver complete analgesia to the fracture site (see ***Calculating Intercostal Sites***, previous page). Count sites multiple times to ensure the appropriate spaces are blocked. While wearing gloves, clip long hair at the injection site if needed for accurate palpation, and clear the site of debris and obvious contamination.



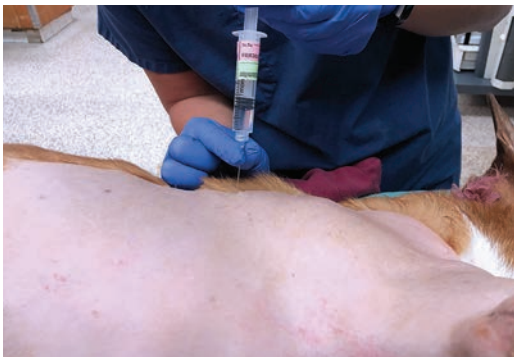
STEP 4

Place the patient in lateral recumbency with the injured side up, and ensure supplemental oxygen is being provided. Insert a small (<22-gauge) spinal needle as dorsally as possible (near the intervertebral foramen) at the very caudal border of the rib cranial to the desired intercostal space.



Author Insight

Mask oxygen is considered adequate if the patient is not receiving additional support (eg, nasal cannulas). If the patient already has a nasal cannula, this is preferred over a mask but does not need to be placed solely for this procedure.



STEP 5

Walk off the rib surface in a caudal direction, then aspirate with a syringe containing a small amount of sterile saline to confirm that the needle is not in a vessel or in the thoracic cavity.

Author Insight

Imaging (eg, ultrasonography, fluoroscopy) can help indicate the correct location.

STEP 6

Inject a small amount of sterile saline. If there is no resistance, disconnect this syringe and connect the syringe of local anesthetic; if resistance is encountered, carefully redirect the needle, using caution not to enter the thoracic cavity. Slowly inject the total volume for the site over 2 minutes. Repeat the process for each additional site. Monitor the patient for changes in respiratory rate/character or signs of respiratory distress that may be indicative of a pneumothorax.

STEP 7

Continue with supplemental oxygen, and perform thoracocentesis if pneumothorax is suspected.

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A New Way to Manage Inappetence in Dogs

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When selecting an appetite stimulant, it is critical to look at pharmacologic management that stimulates appetite as a *main effect*, not side effect, of the drug.

Inappetence is best described as a spectrum with varying degrees of appetite reduction. Although inappetence is most commonly associated with anorexia, it is equally important to recognize and acknowledge hyporexia and dysrexia.[1]

Definitions[1]

- **Anorexia:** A lack of appetite leading to no food intake.
- **Hyporexia:** A decreased appetite leading to decreased food intake.
- **Dysrexia:** A change in appetite that results in an altered food intake.

Assessment

To recognize the form of inappetence, clinicians must take a full medical history and conduct a physical examination to gather vital information. This includes weight history, owner assessment of appetite and behavior changes, and body and muscle condition scores.[2] Nutritional intake should also be recorded, including type and amount of food fed to determine whether the diet is complete or balanced[3] and meets resting and metabolic energy requirements.[4]

Many patients may require assisted feeding, which is any alteration to voluntary eating (eg, using a feeding tube, changing food texture, navigating the patient to food). Although assisted feeding is useful, it can be time-intensive and, in the case of tube feeding, cost-prohibitive for the owner.[5,6] Forced feeding may result in food aversion, aspiration, unnecessary stress, and delay to spontaneous eating (voluntary food intake).[6]

Pharmacologic Options in Dogs

The ability to return to and maintain spontaneous eating is frequently a positive prognostic indicator.[7] Traditional pharmacologic management of appetite stimulation has been through use of drugs that are not primarily indicated for that purpose—and in many cases, with only anecdotal reports of safety and efficacy.[8] The primary goal of extra-label use of these medications is to encourage spontaneous feeding, but there have been no FDA-approved medications labeled for appetite stimulation in dogs before Entyce (capromorelin oral solution) was available in October 2017.[1]

Capromorelin (Entyce) is a ghrelin-receptor agonist that is FDA-approved and indicated for appetite stimulation in dogs.[1] The drug mimics the action of ghrelin, the "hunger" hormone that plays an important role in appetite.[9] Clinical trials support its safe use and efficacy in canine patients with reduced appetite.[1]

Cyproheptadine is an antihistamine used in dogs extra-label as an appetite stimulant. Its mechanism of action is through competition with histamine for H_1-receptor sites and antagonization of serotonin receptors. Cyproheptadine is known to cause sedation and anticholinergic effects.[8]

Maropitant citrate is a neurokinin receptor agonist (NK1) that blocks the action of substance P—a neurotransmitter involved in vomiting—in the central nervous system. It is FDA-approved for the prevention of acute vomiting and the prevention of vomiting in dogs due to motion sickness. Clinicians may use maropitant to enhance food intake in inappetent dogs working under the assumption that these patients are nauseous; however, this is *not always* the case.

Mirtazapine is a tetracyclic antidepressant used extra-label in dogs as an appetite stimulant and/or antiemetic. Little data exist regarding the pharmacokinetics or efficacy of mirtazapine as an appetite stimulant in dogs.[10]

Prednisone/prednisolone is a glucocorticoid used as an anti-inflammatory and anti-neoplastic agent. Side effects of this medication include polyphagia from the hyperglycemic effect of antagonizing insulin, seen in short- and long-term dosing. There are many contraindications and undesirable effects with steroids, including polyuria, polydipsia, and immune suppression.[8]

Conclusion

Early recognition and intervention are key to avoiding detrimental outcomes of decreased appetite. Entyce is the only appetite stimulant FDA-approved for use in dogs.[1]

See page 68 for product information summary.

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Fluid Therapy

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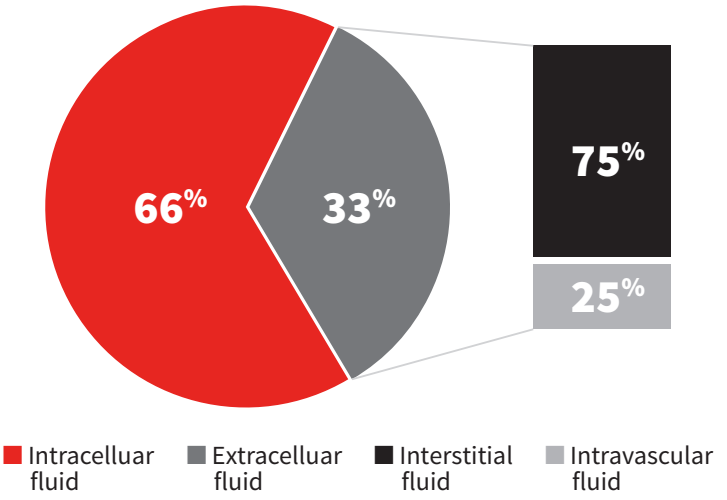
University of Tennessee

Fluid therapy is an essential therapeutic component in small animal practice. Normal cellular function can be impaired without water and potentially lead to patient death.[1] Intravenous fluids may be prescribed to hospitalized patients to treat hypovolemia, dehydration, electrolyte imbalance, and acid-base abnormalities and to ensure that adequate cellular maintenance requirements are met.[2]

Fluid Compartments

Understanding the concept of fluid compartments can help the clinician determine the location of the fluid deficit and appropriate treatment. The body weight of nonobese cats and dogs is composed of approximately 60% water.[2] Puppies and kittens have higher total body water amount (ie, up to 80% of body weight), as total body water decreases with age.[3] In addition, fat has a lower water content; thus, the fluid prescription should be based on estimated lean body weight.[4] In adult nonobese cats and dogs, approximately two-thirds of total body water (ie, 66% of total body water or ≈40% of body weight) is in the intracellular space. The remaining one-third (ie, 33% of total body water or ≈20% of body weight) is in the extracellular space; of this extracellular body water, 75% (≈15% of body weight) is in the interstitial space and 25% (≈5% of body weight) is in the intravascular space (***Figure***, next page). Intracellular fluid loss is generally not appreciated on physical examination and typically manifests as hypernatremia. Treatment of intracellular fluid deficit is beyond the scope of this article.



▲ **FIGURE** Distribution of total body water in an adult nonobese cat or dog

TABLE 1

PHYSICAL & LABORATORY ABNORMALITIES IN PATIENTS WITH HYPOVOLEMIA & DEHYDRATION

Hypovolemia	Dehydration
Tachycardia (bradycardia in terminal stages) in dogs	Dry mucous membranes
Pale mucous membranes	Doughy abdomen
Weak peripheral pulses	Sunken eyes
Altered mentation	Skin tenting
Prolonged capillary refill time	Azotemia
Cold extremities	Elevated hematocrit and total protein
Hypotension	
Elevated lactate	
Hypothermia, bradycardia (heart rate, <160 bpm), and hypotension*	

* Cats tend to demonstrate this triad.

Intravascular fluid deficit (ie, hypovolemia) leads to inadequate oxygen delivery to the cells (ie, poor perfusion or shock). Untreated intravascular fluid deficit can be life-threatening, as oxygen is important for minute-to-minute cellular function maintenance. Inadequate oxygen delivery can lead to hyperlactatemia through anaerobic glycolysis, cell membrane disruption, cell death, and organ death.[5] Physical examination findings of hypovolemia (***Table 1***) include tachycardia in dogs, bradycardia in cats (and in the terminal stages of shock in dogs), prolonged capillary refill time, pale mucous membranes, weak peripheral pulses, cold extremities, and altered mental state. Patients exhibiting these signs require emergent treatment to rapidly restore oxygen delivery. Common clinical conditions that lead to intravascular fluid loss include hemorrhage secondary to trauma, coagulopathy, neoplasia, gastroenteritis, pancreatitis, and peritonitis.

Interstitial fluid deficit (ie, dehydration) is commonly assessed based on a percentage of the estimated interstitial fluid lost (***Table 2***) and typically does not result in life-threatening abnormalities unless dehydration progresses to approximately 9% or greater. Signs of dehydration that may be identified on physical examination include skin tenting, dry mucous membranes, doughy abdomen, and sunken eyes. The different clinical approaches and urgency for treating poor perfusion and dehydration make differentiating between them vital (***Table 1***).

Fluid Types

A crystalloid is a water-based solution composed of osmotically active small molecules that are permeable to the capillary.[6] A significant percentage of crystalloids move into the interstitial and intracellular space within approximately 45 minutes of intravenous administration. Isotonic crystalloids (eg, 0.9% NaCl, lactated Ringer's solution), which are primarily used for fluid therapy in veteri-

nary medicine, have osmolality similar to plasma and therefore do not cause cellular swelling or shrinkage when administered.[6] Hypotonic and hypertonic crystalloids have lower and higher osmolality, respectively, as compared with plasma.

Synthetic colloids (eg, hydroxyethyl starch solutions) are crystalloid-based fluids composed of large molecules that do not cross the capillary membrane. Colloids can be used to treat hypovolemia and/or hypoproteinemia.[7-9] Synthetic colloids should be used cautiously in veterinary patients[10,11] because of concerns in human patients that acute kidney disease and coagulopathies may develop.

Fluid Prescription

A quick stepwise approach that provides an individualized fluid plan for the patient is needed once it has been determined that fluid therapy may be beneficial. Using a fluid prescription consisting of 3 straightforward steps (vs arbitrarily putting a patient on a 2× maintenance fluid rate) ensures that the patient's fluid deficit is identified and corrected in a timely manner (see ***Examples of Individualized Fluid Plans***, page 75). Ongoing fluid losses are not included in this plan but should be replaced in patients with significant ongoing fluid loss (eg, a puppy with parvoviral enteritis with continued vomiting and diarrhea).

Hypovolemia and dehydration can occur independently of each other; therefore, dehydrated patients may not be hypovolemic, and hypovolemic patients may not be dehydrated.

Step 1: Resuscitation (Identify & Treat Hypovolemia if Present)

Hypovolemia can lead to poor oxygen delivery and should be identified (***Table 1***) and treated quickly.[12] If hypovolemia is suspected or identified, fluids should be administered intravenously or via the intraosseous route.

TABLE 2

PHYSICAL EXAMINATION FINDINGS OF DEHYDRATION & ESTIMATE OF FLUID LOSS PERCENTAGE

Dehydration Percentage	Physical Examination Findings
<5%	Dehydration is not clinically detectable, but patient has history of fluid loss
5%-7%	Dry mucous membranes Skin tenting
7%-9%	Dry mucous membranes Skin tenting Sunken eyes Doughy abdomen
9%-12%	Dry mucous membranes Skin tenting Sunken eyes Doughy abdomen Evidence of hypovolemia may be present
12%-15%*	Dry mucous membranes Skin tenting Sunken eyes Doughy abdomen Evidence of hypovolemia is present

* Death is imminent.

Like any drug used in clinical medicine, fluids are not benign, and their use can potentially lead to life-threatening complications.

Fluids administered subcutaneously, in the peritoneal cavity, or through the oral route are not absorbed well because blood flow is diverted to the heart, lungs, and brain in a hypovolemic state. Cats with evidence of hypovolemia should be actively warmed to a body temperature of at least 97°F (36°C) before large volumes of fluids are given.

The shock dose is an estimate of the total blood volume (dogs, 90 mL/kg/hr; cats, 60 mL/kg/hr). It is unlikely that a hypovolemic patient will have lost its entire blood volume; thus, approximately 25% of the fluid prescription (dogs, 20 mL/kg/15 min; cats, 15 mL/kg/15 min[13]) should be administered using pressure bags, fluid pumps, or a 60-mL syringe. Fluid pumps run at 999 mL/hr and are best used for boluses when the total volume to be infused over 15 minutes is less than 250 mL.

The patient should be re-evaluated after the fluid bolus is given. Additional fluid boluses can be administered (dogs, ≤90 mL/kg/hr; cats, 60 mL/kg/hr) if clinical parameters of hypovolemia have improved but are not yet satisfactory (see ***Oxygen Delivery Restoration Parameters***). Fluid administration can be discontinued when the patient has met the desired criteria, but, because isotonic crystalloids have a short lifespan in the intravascular space, the patient's vital parameters should be monitored closely.

Synthetic colloids (eg, hydroxyethyl starch solutions; 1-5 mL/kg every 15 minutes) can be used to treat hypovolemia. The author prefers to use the low end of the dose range for cats, whereas dogs tend to tolerate the higher end.

Step 2: Rehydration (Identify & Treat Dehydration if Present)

After hypovolemia (if present) is treated, the patient should be evaluated (***Table 1***, page 72) and treated for dehydration as needed. The fluid deficit in the interstitial space can be determined by multiplying the patient's body weight by the estimated dehydration percentage (***Table 2***, previous page)[1]:

Fluid deficit (liters) =
weight in kg × % dehydration

The fluid deficit is then replaced over a period of 6 to 24 hours[1] using any isotonic crystalloid. The author prefers to replenish the fluid deficit over 6 to 8 hours except in cats and in patients with underlying heart disease, in which the fluid deficit is replaced over 12 to 24 hours.

Step 3: Maintenance (Provide Cellular Maintenance Requirement)

Cells have a daily water requirement to maintain regular metabolism. Maintenance fluids (dogs, 60 mL/kg/q24h; cats, 45 mL/kg/q24h[12]) can be provided as part of the fluid plan when a patient is not eating or drinking, in addition to correcting dehydration and restoring perfusion. Multiple units of the maintenance dose (rates 2× or more above the maintenance rate) can be provided to patients that may benefit

Continues on page 76

OXYGEN DELIVERY RESTORATION PARAMETERS

- Normal heart rate (dogs, 100-140 bpm; cats, >160 bpm)
- Pink mucous membranes
- Normal capillary refill time (<2 seconds)
- Normal peripheral pulses
- Improved mentation
- Improved blood pressure (100-140 mm Hg systolic)
- Improved serum lactate (1-2.5 mmol/L)

EXAMPLES OF INDIVIDUALIZED FLUID PLANS

EXAMPLE 1

Gerald, a 4-year-old neutered male cat weighing 6.6 lb (3 kg), is presented for vomiting and diarrhea of 3 days' duration. He was anorexic and lethargic prior to presentation.

On physical examination, Gerald is quiet and has a heart rate of 120 bpm, pale mucous membranes with a capillary refill time of about 2 seconds, weak peripheral pulses, initial blood pressure of 50 mm Hg (systolic), and a body temperature of 94°F (34°C). He is also estimated to be about 6% dehydrated based on skin tenting and dry mucous membranes.

STEP 1: RESUSCITATION

Gerald has signs of hypovolemia (ie, bradycardia, hypotension, hypothermia, weak peripheral pulses, pale mucous membranes) and should be resuscitated immediately to restore oxygen delivery.

- A peripheral catheter—or intraosseous catheter if a peripheral catheter is difficult to place—should be used. The medial saphenous veins may be easier to access in hypovolemic cats.
- Exogenous heating (eg, forced air warming devices) should be used to raise body temperature to at least 97°F (36°C).
- A 45-mL (15-mL/kg) balanced isotonic crystalloid (eg, lactated Ringer's solution, 0.9% NaCl) should be administered over 15 minutes using a 60-mL syringe or a fluid pump.
- Parameters should be reassessed and stopped if the patient has met the end goals (see ***Oxygen Delivery Restoration Parameters***).
- As the patient's body temperature rises, additional fluid boluses can be given, if needed.

STEP 2: REHYDRATION

Gerald responded well to the fluid given during resuscitation. His heart rate is now 200 bpm, blood pressure is 100 mm Hg, and mucous membranes are pink. He still has signs of dehydration based on skin tenting and dry mucous membranes and is estimated at 6% dehydration. This fluid deficit should be replaced using an isotonic crystalloid.

- Fluid deficit calculation:
  Fluid deficit (liters) =
  weight in kg (3) × % dehydration (0.06)
  Fluid deficit = 3 × 0.06
  Fluid deficit = 0.18 L (180 mL)
- Timeframe needed to replace the fluid deficit (cats tend to be less fluid tolerant; Gerald's deficit will be replaced over 12 hours):
  180 mL q12h = 15 mL/hr for 12 hours

STEP 3: MAINTENANCE

Hourly fluid requirements (ie, maintenance fluids) should be provided to maintain normal cellular activity. Because the patient is not eating or drinking, the maintenance requirement should be provided using an isotonic crystalloid; a hypotonic crystalloid can also be used to provide maintenance requirements.

- The maintenance fluid requirement is:
  45 mL/kg q24h (45 × 3) = 135 mL/q24h or 6 mL/hr
- Overall fluid prescription after treating hypovolemia is:
  Fluid deficit (15 mL/hr) + maintenance (6 mL/hr) = 21 mL/hr for the first 12 hours; fluid rate is then reduced to 6 mL/hr (provided there are no ongoing fluid losses)

EXAMPLE 2

Sasha, a 4-year-old female Dachshund weighing 15.4 lb (7 kg), is presented for evaluation after being hit by a car. Physical examination findings reveal a heart rate of 160 bpm, pale mucous membranes, a capillary refill time of 3 seconds, and weak peripheral pulses. She has a broken left femur and some abrasions associated with the fracture. The remainder of the findings are within normal limits.

STEP 1: RESUSCITATION

Sasha has signs of hypovolemia (ie, poor perfusion) based on tachycardia, prolonged capillary refill time, and weak peripheral pulses.

- A large-bore intravenous catheter should be placed and fluid therapy initiated to restore oxygen delivery. An analgesic—ideally opioids—should be administered for fracture-associated pain that may also lead to tachycardia.
- A 140-mL isotonic crystalloid bolus should be administered (20 mL/kg) rapidly over 15 minutes. A fluid pump may be used.
- Physical examination parameters should be reassessed to ensure end goals (see ***Oxygen Delivery Restoration Parameters***) have been met after providing a fluid bolus. The crystalloid dose may be repeated up to 90 mL/kg/hr.

STEP 2: REHYDRATION

Physical examination findings consistent with dehydration are not found. This step can be skipped.

STEP 3: MAINTENANCE

Because Sasha is not likely to begin eating or drinking immediately, she will likely benefit from maintenance fluids.

- Maintenance fluid requirement is:
  60 mL/kg q24h (60 × 7) = 420 mL q24h or 18 mL/hr
- Overall fluid prescription after treating hypovolemia is:
  Fluid deficit (0 mL/hr) + maintenance (18 mL/hr) = 18 mL/hr until she starts to eat and drink on her own (provided there are no ongoing fluid losses)

from diuresis (eg, after exposure to toxins). Isotonic crystalloids are typically used to provide maintenance requirements, but hypotonic crystalloids (eg, 0.45% NaCl) may also be used.

Complications of Fluid Therapy

Like any drug used in clinical medicine, fluids are not benign, and their use can potentially lead to life-threatening complications, including respiratory distress secondary to volume overload, coagulopathies, electrolyte abnormalities, acid-base disturbances, and propagation of inflammation.[14] Fluid prescriptions should be individualized and the patient monitored often to detect any adverse effects associated with fluid therapy.

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Use CO_2 Laser to Excise Trichoblastoma

By Christopher Winkler, DVM, Dipl. ABLS

Tumors of the hair follicles include (in decreasing order of frequency) trichoblastomas, trichoepitheliomas, and pilomatrixomas, and account for approximately 5% of all skin tumors in dogs. They arise from the hair germ epithelium, and are generally benign with an excellent prognosis following surgical excision.[1] Their location sometimes results in ulceration and bleeding. The location of the mass can also make such a surgical excision difficult, or the post-operative recovery problematic. Soft tissue cysts and masses between the digits have increased chances of bleeding, due to direct contact with the ground, little available skin to adequately close an incision, and self-mutilation. Such bleeding during the surgery can also obscure the surgeon's view and lead to secondary trauma of underlying structures. Pedal vessels and tendons have little covering for protection.

A CO_2 laser cauterizes blood vessels up to 0.5 mm in diameter as it cuts, allowing excellent visualization of the tissues as the surgery proceeds. The precise incision and hemostasis control the laser provides are especially valuable when care must be taken to watch out for and preserve delicate structures such as the underlying pedal vessels and flexor tendons. Invasive masses may be more easily dissected from such structures with the laser as well. Reduced direct tissue contact and the ability to destroy pathogens decreases infectious contamination. Nerves and lymphatics are also sealed, decreasing post-operative pain, swelling and discomfort, while allowing the pet a faster recovery time with less tendency to self-mutilate.[2]

Case

A 5-year-old spayed female Golden Retriever was referred from her regular veterinarian for a presumed mass of the plantar left hind paw (Figure 1). After unsuccessful attempts to resolve the lesion medically, the case was referred to our clinic for surgical explorationExamination revealed a firm 2 cm cutaneous mass between the plantar metatarsal and digital pads of the left hind paw, which did not palpate as invasive to underlying structures. No open wounds or discomfort on palpation were observed. The decision was made to attempt to remove the mass in its entirety for biopsy.

Anesthesia

The patient was pre-medicated with dexmedetomidine 125 mcg/m² IM, and carprofen 4.4 mg/kg SQ. The patient was induced with propofol 3 mg/kg IV, and general anesthesia was maintained with isoflurane via endotracheal tube.

Laser Equipment

A 20-watt Aesculight surgical CO_2 laser with a flexible hollow waveguide, and handpiece with a removable 0.25 mm ceramic tip (Figure 2) and wide ablation nozzle (Figure 3).

Technique

The patient was positioned in left lateral recumbency with the left hind limb positioned so as to facilitate access, and the operative site was clipped and prepped. The laser was utilized to excise the mass in an elliptical incision, with constant tension being applied to facilitate incision and monitor underlying structures (Figure 2). A smoke evacuator was utilized to draw vaporized debris away from the site, while moistened gauze helped to protect peripheral tissues from thermal injury. The laser offered excellent hemostasis during the procedure and complete excision went without complication (Figure 3 shows the excised mass), or damage to the underlying vessels (Figure 4). The precision of the laser also provided enough skin for adequate closure. A wide ablation nozzle (Figure 5) assisted in ablating uneven skin edges to facilitate complete closure (Figure 6).

Postoperative Care

The patient was administered atipamezole 250 mcg/kg, butorphanol 0.2 mg/kg, and penicillin G procaine 20,000 units/kg IM at surgical recovery. A bandage was applied over the left hind-paw, to be changed within 2-3 days by her regular veterinarian. An Elizabethan collar was used. The patient was discharged home later the same day with cephalexin 500 mg PO BID for 10 days, and carprofen 12.5 mg PO BID for 7 days.

A biopsy found the mass to be a trichoblastoma, with no evidence of vascular or lymphatic invasion. Removal of the mass was complete and was expected to be curative.

Special thanks to Molly Miosek, DVM, of Dr. Molly's Vet Clinic, Montauk NY

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FIGURE 1. Mass immediately preoperatively

FIGURE 4. The underlying pedal vessels are undamaged.

FIGURE 2. Surgical removal in an elliptical fashion using a 0.25-mm ceramic tip

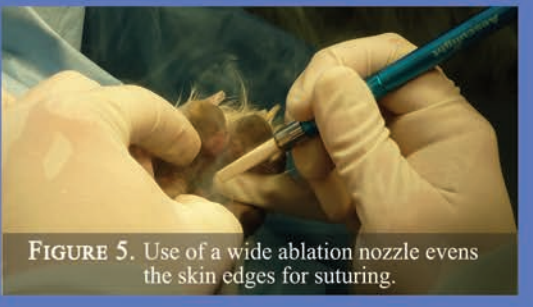

FIGURE 5. Use of a wide ablation nozzle evens the skin edges for suturing.

FIGURE 3. The excised trichoblastoma

FIGURE 6. Use of a wide ablation nozzle evens the skin edges for suturing.

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About Dr. Winkler:

Dr. Winkler, a 2001 graduate of the Ross University School of Veterinary Medicine, owns Suffolk Veterinary Group Animal Wellness and Laser Surgery Center in Selden, N.Y. He uses CO_2 and diode laser wavelengths in his practice, often combining them when possible. He is a member of the American Society for Laser Medicine and Surgery and has appeared as an associate instructor on CO_2 laser surgery at national veterinary conventions. He is available for consultation and training in small animal laser surgery and laser therapy.

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QUIZ CORNER

QUIZ YOURSELF

on this issue's features

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1 **CASE ROUTES** PAGE 17

In patients with pre-existing ocular hemorrhage, which of the following might be contraindicated?

A. Mydriatic cycloplegics (eg, atropine ophthalmic solution)
B. Topical corticosteroids
C. Ocular ultrasonography
D. Intraocular injections

2 **TOP 5** PAGE 35

What is the most common abnormality seen on serum chemistry profile results of dogs with hyperadrenocorticism?

A. Increased alanine transaminase
B. Increased alkaline phosphatase
C. Hyperglycemia
D. Hypercholesterolemia

3 **CASE IN POINT** PAGE 39

Which of the following is *not* true regarding neuropathic pain?

A. Neuropathic pain is caused by a lesion or disease of the somatosensory system.
B. Clinical presentation includes allodynia and hyperalgesia.
C. Diagnosis is easily made based on presence of specific clinical signs.
D. Treatment usually requires a multimodal approach for analgesia.

4 **PROCEDURES PRO** PAGE 62

When performing an intercostal block for rib fractures, block at least ____ intercostal space(s) cranial to and caudal to the fracture on the ipsilateral side.

A. 1
B. 2
C. 3
D. 4

5 **CONSULT THE EXPERT** PAGE 71

A clinical presentation of dry mucous membranes and skin tenting, with no further signs of dehydration, would be indicative of approximately what percentage of fluid loss?

A. <5%
B. 5% to 7%
C. 7% to 9%
D. 9% to 12%

1: D 2: B 3: C 4: B 5: B

POLLING PLACE

WE ASKED ...

How do you prepare for and handle emergency presentations? (Check all that apply)

YOU ANSWERED ...

A. Maintain a fully stocked crash cart 29%
B. Provide in-house education on emergency medicine and critical care 22%
C. Have dedicated staff for handling emergencies 15%
D. Keep some appointment slots open to accommodate emergencies 18%
E. Stabilize then refer all emergencies to a local emergency clinic 16%

THIS MONTH'S QUESTION ...

What clinical sign and/or abnormality has led you to suspect Addison's disease in a patient? (Check all that apply)

A. Eosinophilia
B. Chronic GI disease
C. Weakness
D. Hypoglycemia
E. Sodium:potassium ratio <27
F. Increased BUN:creatinine ratio
G. Lack of stress leukogram in a sick dog

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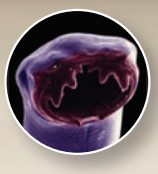
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