RESPONSIBLE
ANTIMICROBIAL
STEWARDSHIP

IN THIS ISSUE

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Respiratory Noise in a Labrador Retriever

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**Local anesthetic**
Single use vial

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**Dosage and Administration:**
NOCITA is for single dose administration only. A dose of 5.3 mg/kg (0.4 mL/kg) is administered by infiltration injection into the tissue layers at the time of incisional closure for dogs. A single dose administered during surgical closure may provide up to 72 hours of pain control.

**Contraindications:**
Do not administer by intravenous or intra-articular injection. If accidental intravascular administration occurs, monitor for cardiovascular (dysrhythmias, hypotension, hypertension) and neurologic (tremors, ataxia, seizures) adverse reactions. Do not use for intra-articular injection. In humans, local anesthetics administered into a joint may cause chondrolysis.

**Warnings:**
Not for use in humans. Keep out of reach of children. NOCITA is an amide local anesthetic. In case of accidental injection or accidental topical exposure, contact a physician and seek medical attention immediately. Wear gloves when handling vials to prevent accidental topical exposure.

**Precautions:**
Do not administer concurrently with bupivacaine HCl, lidocaine or other amide local anesthetics. A safe interval from time of bupivacaine HCl, lidocaine or other amide local anesthetic administration to time of NOCITA administration has not been determined. The toxic effects of these drugs are additive and their administration should be used with caution including monitoring for neurologic and cardiovascular effects related to toxicity.

The safe use of NOCITA in dogs with cardiac disease has not been evaluated.

The safe use of NOCITA in dogs with hepatic or renal impairment has not been evaluated. NOCITA is metabolized by the liver and excreted by the kidneys. The ability of NOCITA to achieve effective anesthesia has not been studied. Therefore, NOCITA is not indicated for pre- incisional or pre-procedural loco-regional anesthetic techniques that require deep and complete sensory block in the area of administration.

The safe use of NOCITA in dogs for surgical procedures other than cranial cruciate ligament surgery has not been evaluated.

The safe use of NOCITA has not been evaluated in dogs younger than 5 months old.

The safe use of NOCITA has not been evaluated in dogs that are pregnant, lactating or intended for breeding.

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US Patent: 8,182,835; 8,834,921; 9,205,052
From Clinician’s Brief on Social Media

WE ASKED …

How many times did you apply to veterinary school before being accepted?

“3 times, and I was always the first alternate. On my self-declared ‘last time,’ someone declined their admission and I was accepted.”—Jillaine P

“5 times! I needed to learn patience and perseverance first.”—Danielle C

“3 times. The first 2 times, I only applied to the school in my state. The third time, I applied to 6 out-of-state schools and to University of Glasgow in the United Kingdom. I received offers from 1 of the out-of-state schools and from Glasgow. I am proud to say I am a graduate of University of Glasgow!”—Ashley B

“I applied and was accepted on my first try. Sometimes I still cannot believe it. I feel incredibly fortunate to be part of this profession.”—Chantelle K

“Twice! I almost did not reapply, but, thankfully, my brother gave me a pep talk and I did. I love my job; it has its moments, but it is my world!”—Ashley B

“Once, and I applied to 15 programs. ‘All or nothing,’ I said.”—Erica U

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41% No

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WE ALL HAVE THOSE DAYS …

I got halfway through my grocery list before realizing that I had initialed every item I crossed off.

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**Cranial cruciate ligament**

**DOG INDICATION:** For single-dose infiltration into the surgical site to provide local postoperative analgesia for cranial cruciate ligament surgery in dogs.

**CAT INDICATION:** For use as a peripheral nerve block to provide regional postoperative analgesia following onychectomy in cats.

**IMPORTANT SAFETY INFORMATION:** NOCITA® (bupivacaine liposome injectable suspension) is for use in dogs and cats only. Do not use in dogs or cats younger than 5 months of age, that are pregnant, lactating or intended for breeding. Do not administer by intravenous or intra-arterial injection. Adverse reactions in dogs may include discharge from incision, incisional inflammation and vomiting. Adverse reactions in cats may include elevated body temperature, infection or chewing/licking at the surgical site. Avoid concurrent use with bupivacaine HCl, lidocaine or other amide local anesthetics. See page 2 for product information summary. Please see the full Prescribing Information at nocita.aratana.com for more detail.

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* Cranial cruciate ligament

**DOG INDICATION:** For single-dose infiltration into the surgical site to provide local postoperative analgesia for cranial cruciate ligament surgery in dogs.

**CAT INDICATION:** For use as a peripheral nerve block to provide regional postoperative analgesia following onychectomy in cats.

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CASE IN POINT
Anorexia & Lethargy in a Dog with Presumed Giardiasis
Ali Nemeth, DVM
Orla Mahony, MVB, DACVIM, DECVIM (CA)
Nketa Kakar, DVM
Claire L. Fellman, DVM, PhD, DACVIM, DACVCP

CONSULT THE EXPERT
Monitoring Blood Glucose in Patients with Diabetes Mellitus
Thomas Schermerhorn, VMD, DACVIM (SAIM)

DIFFERENTIAL DIAGNOSIS
Hyperkalemia
Julie Allen, BVMS, MS, MRCVS, DACVIM (SAIM), DACVP

CASE IN POINT
Dysphonia & Respiratory Noise in a Labrador Retriever
Bryden J. Stanley, BVMS, MANZCVS, MRCVS, MVetSc, DACVS

NOTICE OF CORRECTION
In the article “Osteosarcoma in a Dog,” published in the February 2018 issue of Clinician’s Brief, the term illectomy should have been used in place of ileectomy. Clinician’s Brief regrets the error.

RED LIGHT, GREEN LIGHT
Juvenile Generalized Demodicosis in a Dog
Andrew Rosenberg, DVM, DACVD
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Dr. Anthony Caiafa
BVSc BDSc MACVSc (SA Surgery and Veterinary Dentistry)
CONTINUING EDUCATION
April Collection
In this CE lesson reflecting the topics published in the April 2019 edition of Clinician’s Brief, discover current recommendations for treating suspected marijuana ingestion, ectoparasites in rabbits, and dogs that are seropositive for Lyme disease but lack clinical signs. brief.vet/aprilCE

PODCAST
Oral Ulcerations with Dr. Bellows
In this episode, Jan Bellows, DVM, FAVD, DAVDC, DABVP, details what signs should raise suspicion for oral ulcers and outlines the appropriate steps to assess these cases. brief.vet/ulceration
Continues on page 67

JULIE ALLEN, BVMS, MS, MRCVS, DACVIM (SAIM), DACVP, is a former clinical assistant professor of clinical pathology at Cornell University. She earned her veterinary degree from University of Glasgow and her MS from Iowa State University, where she completed a rotating internship in small animal medicine and surgery and a residency in small animal internal medicine. She also completed a residency in clinical pathology at North Carolina State University. Dr. Allen focuses on cachexia/anorexia, endocrinology, and hepatobiliary and pancreatic disease and has committed her career to improving the diagnosis of disease.

DIFFERENTIAL DIAGNOSIS PAGE 37

CLAIRES L. FELLMAN, DVM, PhD, DACVIM, DACVCP, is an assistant professor of small animal internal medicine and clinical pharmacology at Cummings School of Veterinary Medicine at Tufts University. Dr. Fellman completed her clinical training at and earned her PhD from Mississippi State University, where she helped develop assays to measure the effects of cyclosporine on T cells in dogs. Her interests include immunology, pharmacology, and antimicrobial stewardship.

CASE IN POINT PAGE 17

NEKETA KAKAR, DVM, is a small animal internal medicine resident at Foster Hospital for Small Animals in North Grafton, Massachusetts. She earned her DVM from Western University of Health Sciences and completed a small animal rotating internship at Friendship Hospital for Animals in Washington, DC. Her interests include nephrology, hematology, and immunology.

CASE IN POINT PAGE 17

JILL MADDISON, BVSc, DipVetClinStud, PhD, FACVS, SFHEA, MRCVS, is Professor of General Practice, Director of Professional Development, and the BVetMed and CertAVP course director at Royal Veterinary College. She is also the small animal clinical program director for London Vet Show and a consultant at a local veterinary practice and at Beaumont Sainsbury Animal Hospital in London. Professor Maddison is the senior editor of the second edition of Small Animal Clinical Pharmacology and the senior editor of Clinical Reasoning in Small Animal Practice. She has lectured worldwide on clinical problem-solving, small animal internal medicine, and clinical pharmacology.

CONSULT THE EXPERT PAGE 11

ORLA MAHONY, MVB, DACVIM, DECVIM (CA), is a clinical assistant professor of small animal internal medicine at Cummings School of Veterinary Medicine at Tufts University. Her interest is endocrinology.

CASE IN POINT PAGE 17
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* Data on file.

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Fortunately, most infected dogs have no clinical signs or only mild signs of heartworm disease (HWD) and tend to undergo adulticide therapy with few major complications. The likelihood of complications associated with HWD increases with the chronicity of infection. Prognosis is dependent on stabilization, the ability to administer subsequent adulticide therapy and the ability of the family to commit to treatment of chronic conditions.

Following is a brief overview of these complications, including clinical signs, diagnosis and treatment. For information on drug dosages, please visit [www.heartwormsociety/treating-severe-HWdisease](http://www.heartwormsociety/treating-severe-HWdisease).

**PNEUMONITIS**
What it is: Inflammation in the pulmonary parenchyma due to HWD
Cause: Death of microfilaria and/or the presence of adult worms
Common clinical signs: Cough, tachypnea
How to diagnose: Radiographs typically show unstructured interstitial infiltrate
Treatment: Steroid therapy, rest and oxygen as needed

**PULMONARY HYPERTENSION (PH)**
What it is: Increased pulmonary vascular resistance and obstruction
Cause: Chronic, untreated HWD leads to pulmonary vascular endothelial injury, remodeling, and dysfunction; physical obstruction by worms also contributes
Common clinical signs: Lethargy, shortness of breath, cyanosis and/or syncope
How to diagnose: Echocardiographic evidence of right-heart remodeling ± estimation of pulmonary pressures if tricuspid or pulmonary valve insufficiencies present
Treatment: Sildenafil, rest and oxygen as needed; anticoagulant therapy when there is high suspicion of HW-PTE (e.g. cyanosis and collapse 3-21 days after adulticide or visualization of thrombus) and no contraindications

**HW-PTE**
What it is: Thrombus formation from dead and dying worms; thrombi and worm fragments may stay in place or embolize
Cause: Worm death, which may occur 3-21 days after adulticide administration or spontaneously
Common clinical signs: Lethargy, shortness of breath, cyanosis and/or syncope
How to diagnose: Echocardiographic assessment for PH, which is usually present (see above); rarely may see thrombus in pulmonary trunk or branches
Treatment: Sildenafil, rest, corticosteroids and oxygen if needed; anticoagulant therapy when there is high suspicion of HW-PTE (e.g. cyanosis and collapse 3-21 days after adulticide or visualization of thrombus) and no contraindications

**RIGHT-SIDED HEART FAILURE (R-HF)**
What it is: PH puts chronic pressure load on the right heart, leading to right ventricular failure
Common clinical signs: Lethargy, abdominal distension, shortness of breath, jugular venous distension and/or pulsation, syncope
How to diagnose: Echocardiography shows right-sided heart remodeling; presence of transudate or modified transudate cavitary effusions
Treatment: Mechanical removal of effusions, diuretic, pimobendan, and sildenafil (to treat underlying PH); also consider spironolactone and/or angiotensin-converting-enzyme inhibitor

**CAVAL SYNDROME**
What it is: PH and decreased right ventricular function allow worms to relocate to the right heart and cavae
Cause: Worms cause disruption of the tricuspid valve and/or cavae, decreasing venous return to the right heart, reducing stroke volume and cardiac output; worm mass can also lead to microangiopathic anemia and pigmenturia
Common clinical signs: Lethargy, right-sided systolic murmur, syncope, collapse, pallor and pigmenturia
How to diagnose: Clinical signs of above in dogs known to be heartworm+
Treatment: Stabilization (IV fluids, vasopressors, blood products), worm extraction, and management of specific related issues (e.g. pneumonitis, PH or R-HF)

For more information, visit [heartwormsociety.org](http://heartwormsociety.org)
Antimicrobial resistance is a substantial threat to human health. Annually, ≈700,000 humans die of drug-resistant microbial infections; this number could rise to 10 million by 2050 unless current antimicrobial drug use trends are reversed.\(^1\)

Bacterial resistance as a cause of therapeutic failure is less recognized in veterinary medicine because many clinicians in general practice do not have experience caring for patients with drug-resistant UTIs or drug-resistant skin or wound infections.

Antimicrobial drugs are frequently prescribed for companion animals. A study surveying the records of dogs and cats over a 2-year period at a subset of clinics in the United Kingdom found that 25% of dogs and 21% of cats received antimicrobial treatment.\(^2\) Of the antimicrobial drugs administered, 34% of those given to cats and 6% of those given to dogs were drugs determined by the World Health Organization to be of critical importance to human health (ie, fluoroquinolones, macrolides, third-generation cephalosporins).\(^2,3\)

Methicillin-resistant *Staphylococcus pseudintermedius* can be resistant to all antimicrobial drugs used in veterinary medicine, and many other pathogenic organisms (eg, methicillin-resistant *S aureus*, extended-spectrum β-lactamase–producing *Escherichia coli*, carbapenemase-producing *E coli* and *Klebsiella pneumoniae*, multidrug-resistant enterococci) can colonize and infect both farm and companion animals.\(^4\) Because pet owners and veterinary staff have close connections with companion animals, there is also an increased risk for organism transfer between species\(^5-7\); young children and immunocompromised pet owners are at the greatest risk.
Responsible antimicrobial stewardship reduces inappropriate antimicrobial use, improves appropriate antimicrobial use, and reduces the risk for transfer of drug-resistant pathogens between humans and animals.

**How Does Bacterial Resistance Develop?**

Bacterial resistance did not start with the discovery of penicillin. Antimicrobial-resistance mechanisms developed in bacteria >2 billion years ago. Antimicrobial drugs preferentially target resistant populations of bacteria. Selection and clonal amplification of resistant bacterial strains are more likely to occur at sites associated with lower and variable antimicrobial concentrations (ie, sites other than the infection site)—either the gut and skin microbiome or the inanimate environment following excretion of the therapeutic agent or its metabolic breakdown products. Resolution of infection following antimicrobial therapy does not indicate resistance has not occurred. Resistance always occurs to some degree in the normal flora in the skin and gut but can also emerge at the site of infection if treatment was inadequate or inappropriate.

The microbiome is the collection of microorganisms living in or on a human or animal body. A healthy immune system is able to keep the microbiome in balance. Understanding the impact antimicrobial use has on the microbiome is crucial to comprehending the effects of prescribing antimicrobial drugs inappropriately. Human and animal immune systems have developed the ability to cohabit with and control microbiota. Dysbiosis occurs when control of these microbiota is lost. The structure of the microbial community can be influenced by various factors (eg, host genetics, diet, infection, antimicrobial use). Many antimicrobial drugs have long-lasting effects, which can lead to permanent loss of some organisms and proliferation and persistence of other bacteria.

A substantial increase in chronic inflammatory and autoimmune disorders in humans has been attributed, at least in part, to the use of antimicrobial drugs, changes in diet, and a reduction in intestinal parasitism. These changes have profoundly affected human microbiota and, as a direct result, the immune system and are believed to be a factor in a variety of diseases associated with abnormal immune responses toward environmental antigens and self-antigens (eg, inflammatory bowel disease, multiple sclerosis, type 1 diabetes, allergies, asthma). It is not yet known if similar changes are occurring in animals. The prevalence of antimicrobial use in companion animal practice may contribute to the increase in potentially resistant bacteria in the microbiome of pets and pet owners and the increased risk for immune-related disorders in pets.

**Choosing Appropriate Antimicrobial Therapy**

Antimicrobial therapy should eliminate infectious organisms without harming the host and is most effective when supplementing endogenous defense mechanisms rather than acting as the sole means of infection control. The patient’s natural defense mechanisms (eg, mucociliary escalator in the respiratory tract, flushing effect of urination, unique defenses of the microbiome) are of primary importance in preventing and/or controlling infections.

Antimicrobial therapy should be used only if a bacterial infection is a likely diagnosis or has been definitively diagnosed and should not be prescribed in place of a diagnosis. If antimicrobial therapy is used for prophylaxis (eg, perioperatively), the nature of the likely infecting organism should be carefully considered and an appropriate antimicrobial therapy chosen.

Antimicrobial therapy may not be needed for many common clinical presentations that rarely have a bacterial cause, such as in dogs with acute vomiting (with or without diarrhea) caused by dietary indiscretion. In addition, antimicrobial therapy may not be needed in healthy dogs with diarrhea that contains fresh blood (unless an infectious cause is suspected); routine use of metronidazole in these patients has not been shown to be effective.
In young cats (<10 years), signs of lower urinary tract disease are more likely to be caused by stress and calculi, which should not require antimicrobial therapy. Although no good evidence-based studies have been conducted, routine antimicrobial therapy in dogs and cats before, during, and/or after treatment for periodontal disease is typically not justified; scaling, polishing, and extractions (when necessary) are generally sufficient in these patients. Healthy cats and dogs undergoing routine surgical procedures <90 minutes in duration, that do not involve the respiratory or GI tracts, and in which asepsis has been properly maintained do not typically warrant antimicrobial therapy; if prophylactic perioperative antimicrobial therapy is indicated, continuation of therapy for >24 hours postoperatively is typically not necessary unless there is evidence of infection.

Culture & Susceptibility Testing
Culture and susceptibility testing should always be performed in patients with life-threatening infections and/or deep or complex skin infections. Cultures should also be submitted if rod-shaped bacteria are seen on cytology (ie, skin, ears, urine), when empiric antimicrobial drugs are not effective, and when the risk for antimicrobial resistance is high.

Empiric Use
Although culture and susceptibility testing should ideally be performed before antimicrobial therapy is initiated, it may not be practical (often due to economic reasons). In these situations, an empiric choice should be made based on which pathogenic organisms are most likely present at the infection site. Culture and susceptibility testing are strongly recommended if therapy fails or infection immediately recurs after therapy has ceased. When possible, a gram stain should be performed on the exudate and microscopy performed on urine sediment to determine whether gram-positive or gram-negative bacteria are present, as these characteristics may influence empiric prescribing choices.

ANTIMICROBIAL PRESCRIBING CONSIDERATIONS
- Is the bacterial infection confirmed or probable?
- Will the infection cause critical illness?
- Will the infection progress without treatment?
- Is the patient’s condition life-threatening, and can bacterial infection not be ruled out? Pyrexia and neutrophilia may indicate a bacterial infection, but they can also occur with stress, nonbacterial infections (eg, viral, fungal), immune-mediated inflammation, and neoplasia.
- Can the type of infection and antimicrobial susceptibility be predicted? The location of the infection and likely causal pathogens should be considered (eg, gram-negative aerobes and Staphylococcus spp for uncomplicated UTIs, S pseudintermedius for skin infections). Appropriate guidelines should be reviewed (see Suggested Reading, next page).
- Is culture and susceptibility testing indicated and feasible for the patient? Can the infection site be accessed? Is the pet owner able to pay for testing?
- Will the drug’s pharmacokinetic properties influence effectiveness (eg, can the drug get to the infection site)?
- Will infection-site factors (eg, purulent material, necrotic tissue, foreign material) impair drug action? How can infection-site factors be managed to enhance drug efficacy?
- Does the drug have any potential adverse effects for the patient? Patient species, breed, age, and concurrent disease should be considered.
- Is the pet owner able to administer the drug appropriately? Pet owners should understand dosage instructions, be able to administer prescribed medications, remain involved in treatment decisions, and be aware of the adverse effects of poor compliance with medication instructions.
Empiric antimicrobial therapy is necessary for immediate treatment of life-threatening infections until culture results are received. An empiric approach is also appropriate for topical therapy.

Empiric antimicrobial therapy should only be used to treat other infections when the infection is not life threatening, the patient has not had an infection in the past 3 months, skin infection is superficial, the infection has a predictable antimicrobial susceptibility, and the patient does have signs of antimicrobial resistance.15

**Signs of Antimicrobial Resistance**

Antimicrobial resistance, or the risk that it may occur, should be suspected if a patient has received multiple broad-spectrum antimicrobial courses or antimicrobial treatment within the past 3 months. Signs of resistance include nonhealing wounds, postoperative infection, nosocomial infection, and ongoing infection in patients receiving continuing antimicrobial treatment. Urinary calculi, foreign bodies, and/or the need for surgical drainage can also impair therapy. See *Antimicrobial Prescribing Considerations*, previous page, for a comprehensive list of considerations for prescribing antimicrobials.

**Conclusion**

Practicing responsible antimicrobial stewardship involves striving to prevent both antimicrobial resistance and an unnecessary impact on the microbiome by prescribing appropriate drugs to treat infections and recognizing when antimicrobial treatment and prophylaxis are inappropriate. Resistance can occur at infection sites when treatment is inadequate or inappropriate. Resistance can also affect other sites (eg, the microbiome), which can result in the transfer of drug-resistant bacteria and dysbiosis.

**References**


**Suggested Reading**


IMPORTANT SAFETY INFORMATION: For oral use in dogs only. Not for human use. Keep out of reach of children. If accidentally ingested by humans, contact a physician immediately.

The most commonly reported side effects were vomiting, loss of appetite, diarrhea, excessive salivation, agitation, tiredness, vocalization, confusion, increased water consumption, weight loss, weakness, fever, panting, and reversible changes in skin color (flushing or bright pink). Abnormal gait, seizures or tremors, as well as liver enzyme elevations, kidney failure, blood in urine and urine retention have been reported. In some cases death, including euthanasia has been reported. Sudden death was sometimes preceded by vocalization or collapse.

Instances of dogs chewing through closed vials of PROIN® and eating the vial contents have been reported, in some cases resulting in overdose. Keep the product in a secured storage area out of the reach of pets in order to prevent accidental ingestion or overdose, as dogs may willingly consume more than the recommended dosage of PROIN Chewable Tablets or PROIN ER™ tablets. Contact your veterinarian immediately if the dog ingests more tablets than prescribed or if other pets ingest PROIN Chewable Tablets or PROIN ER tablets.

PROIN and PROIN ER may cause elevated blood pressure and should be used with caution in dogs with pre-existing heart disease, high blood pressure, liver disease, kidney insufficiency, diabetes, glaucoma, and other conditions associated with high blood pressure. Dogs may transition from PROIN Chewable Tablets to PROIN ER without a break in administration. However, do not alternate PROIN ER with PROIN Chewable Tablets because the effectiveness and safety of interchangeable use have not been evaluated.

The safe use of PROIN and PROIN ER in dogs used for breeding purposes, during pregnancy or in lactating bitches, has not been evaluated. Contact your veterinarian if you notice restlessness or irritability, loss of appetite, the incontinence persists or worsens, or any other unusual signs. See prescribing information for complete details regarding adverse events, warning and precautions or visit prnpharmacal.com.
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Anorexia & Lethargy in a Dog with Presumed Giardiasis

Ali Nemeth, DVM  
*Tufts Veterinary Emergency Treatment & Specialties  
Walpole, Massachusetts*

Orla Mahony, MVB, DACVIM, DECVIM (CA)  
Neketa Kakar, DVM  
Claire L. Fellman, DVM, PhD, DACVIM, DACVCP  
*Cummings School of Veterinary Medicine at Tufts University*

Rylie, a 7-year-old, 48.4-lb (22-kg), spayed German shorthaired pointer, was initially presented to her primary veterinarian for anorexia and lethargy. She had experienced a self-limiting episode of vomiting and diarrhea 2 weeks before presentation. Rylie was up to date on vaccines and flea and tick preventives and had no pertinent travel history.

Three months prior to presentation, Rylie’s housemate, Henderson, a 2-year-old, 42.8-lb (19.4-kg), neutered male Labrador retriever crossbreed, was diagnosed with *Giardia* spp infection. Although fecal testing had not been performed for Rylie on Henderson’s diagnosis, both dogs were prescribed fenbendazole, a broad-spectrum benzimidazole anthelmintic, at 60 mg/kg every 24 hours for 3 days.

Subsequently, when the owner observed diarrhea in either Rylie or Henderson, deworming was repeated in both dogs with fenbendazole obtained from an online pharmacy. Accordingly, Rylie received a second course of fenbendazole 2 months later at 60 mg/kg every 12 hours for 5 days and a third course a month after the second course at 60 mg/kg every 12 hours for 7 days. The final course of fenbendazole was completed 2 days before Rylie was initially presented to her primary veterinarian.
Initial Diagnostics & Treatment
Physical examination demonstrated a BCS of 3/9 and 5% dehydration. Rylie’s temperature was normal (101.6°F [38.7°C]). CBC and serum chemistry results revealed 1518 neutrophils/µL (reference range, 2060-10,600/µL) and 572 lymphocytes/µL (reference range, 690-4500/µL). Results of point-of-care testing for heartworm disease, Lyme disease, anaplasmosis, and ehrlichiosis were negative. Rylie received lactated Ringer’s solution (500 mL SC) as an outpatient for supportive care of dehydration. Lethargy improved, and her temperature remained normal for 2 days before she became anorexic and markedly lethargic with a temperature of 105.2°F (40.7°C), at which point her owner presented her to an emergency clinic.

Emergency Presentation
Rylie was hospitalized, and blood and urine samples were obtained for CBC, serum chemistry profile, urinalysis, urine culture and susceptibility testing, blood gas analysis, and PCR testing for infectious and tick-borne diseases.* Abdominal radiographs revealed heterogeneous material, presumed to be food, in the gastric lumen and increased small intestinal gas consistent with diffuse gastroenteritis. Abdominal sonograms revealed a moderate decrease in corticomedullary distinction in both kidneys; no other abnormalities were noted.

CBC and serum chemistry profile revealed 100 leukocytes/µL (reference range, 5050-16,760/µL), 10 neutrophils/µL (reference range, 2950-11,640/µL), 70 lymphocytes/µL (reference range, 1050-5100/µL), 20 monocytes/µL (reference range, 160-1120/µL), 67,000 platelets/µL (reference range, 148,000-484,000/µL). Hematocrit was normal (41.8%; reference range, 37.3%-61.7%). Urinalysis showed trace proteinuria with inactive sediment.

Treatment with ampicillin/sulbactam (30 mg/kg IV every 8 hours) and enrofloxacin (5 mg/kg IV every 24 hours) was initiated, pending results of urine culture and susceptibility and PCR testing. Supportive care included IV fluids and antiemetics. Rylie’s temperature remained above 104°F (40°C), and she was emergently referred to a specialty service for further diagnostic investigation and treatment.

Emergency Referral
On admission to the referral service, Rylie’s temperature was 103.4°F (39.7°C). Heart and respiratory rates were within normal limits. No other significant findings were noted on physical examination.

Packed cell volume, total solids, and blood glucose and lactate concentrations were within normal limits. CBC with pathologist review showed 570 leukocytes/µL (reference range, 4400-15,100/µL), 6 neutrophils/µL (reference range, 2800-11,500/µL), 560 lymphocytes/µL (reference range, 1000-4800/µL), 10 monocytes/µL (reference range, 100-1500/µL), and 17,000 platelets/µL (reference range, 173,000-486,000/µL). Hematocrit was in the low-normal range (39%; reference range, 39%-55%), and rare eccentrocytes, 1+ acanthocytes, 1+ to 2+ crenation, occasional keratocytes, and 2+ poikilocytes were seen. No abnormalities were noted on 3-view thoracic radiographs with radiologist review. Bone marrow and core biopsies both revealed a cell population composed almost entirely of adipocytes, with only rare hematopoietic precursor cells; these findings were consistent with generalized bone marrow hypoplasia/aplasia, although aspiration of an area of inactive marrow could have had a similar appearance. However, if the bone marrow sample was representative, Rylie would likely exhibit a decreased hematocrit/nonregenerative anemia in the near future, as erythrocytes are typically the last cell line to decrease following decreased hematopoiesis.

*PCR testing for infectious and tick-borne disease for both Rylie and Henderson included Anaplasma spp, Babesia spp, Bartonella spp, Blastomyces dermatitidis, Brucella canis, Coccidioides spp, Cryptococcus spp, Ehrlichia spp, Hepatozoon spp, Histoplasma capsulatum, Leishmania spp, Leptospira spp, Mycoplasma hemocallis, Mycoplasma haemofelis, Neorickettsia risticii, Neospora caninum, Rickettsia rickettsii, Toxoplasma gondii, and Trypanosoma cruzi.
Differential diagnoses for generalized bone marrow hypoplasia/aplasia are numerous and can include infectious disease (eg, anaplasmosis, ehrlichiosis, canine parvovirus), bone marrow necrosis (eg, from endotoxins or toxins), and myelophthisic disease (eg, myelofibrosis, neoplasia). Other causes can include hemophagocytic syndrome, malignant histiocytosis, hypersplenism, radiation damage, cobalamin deficiency, immune-mediated disease, and pancytopenia from drugs such as estrogen, chemotherapeutic agents, phenylbutazone, meclofenamic acid, trimethoprim/sulfadiazine, quinidine, thiacetarsamide, captopril, albendazole, and cephalosporins. 1-3

Diagnostic imaging and bone marrow evaluation showed no evidence of neoplasia, urine culture results were negative, and results of prior infectious and tick-borne disease testing were negative; therefore, fenbendazole-associated bone marrow suppression was strongly suspected.

**DIAGNOSIS:**
**PRESUMPTIVE BONE MARROW HYPOPLASIA/APLASIA SECONDARY TO FENBENDAZOLE ADMINISTRATION**

**Treatment**
Due to Rylie’s marked neutropenia, ampicillin/sulbactam (30 mg/kg IV every 8 hours) and enrofloxacin (5 mg/kg IV every 24 hours) were continued (see Treatment at a Glance). Doxycycline (5 mg/kg PO every 12 hours) was initiated but discontinued, as results of infectious and tick-borne disease testing were negative.

Rylie tolerated treatment well. She began eating readily, her temperature returned to normal limits, and her vital signs remained within normal limits. She was discharged 24 hours after presentation to reduce the risk for hospital-acquired infection. Enrofloxacin (5 mg/kg PO every 24 hours) was continued at home, and ampicillin/sulbactam was substituted with amoxicillin/clavulanic acid (16.7 mg/kg PO every 12 hours for 14 days). Because bone marrow disease may be immune mediated, prednisone (1.8 mg/kg PO every 24 hours) was also initiated.

**Outcome**
Rylie’s clinical signs resolved quickly. CBC performed 3 days postdischarge showed normal neutrophil and platelet counts and 700 lymphocytes/µL (reference range, 1000-4800/µL).

At the recheck examination 12 days after initial emergency referral, Rylie’s owner noted that Henderson was undergoing treatment for recurrent fever. Henderson had become febrile (104.5°F [40.3°C]) a month earlier after his second course of fenbendazole. He was presented to an emergency service and received fluids (500 mL SC) and amoxicillin (250 mg PO every 12 hours), which the owner discontinued after 5 days.

**TREATMENT AT A GLANCE**

- When bone marrow suppression is present, drug toxicity should be considered and myelosuppressive medications discontinued.
- Animals with bone marrow suppression are at risk for acquiring severe, life-threatening infection, and appropriate broad-spectrum antibiotic therapy is recommended when severe neutropenia of <500 neutrophils/µL is identified. 4
- Serial CBCs should be obtained postdischarge to monitor response to therapy and ensure complete recovery of all cell lines.

When bone marrow suppression is present, drug toxicity should be considered and myelosuppressive medications discontinued.
Henderson became febrile again (103.5°F [39.7°C]) following his third course of fenbendazole. CBC results showed 0 neutrophils/µL (reference range, 2000-12,000/µL) and 138,000 platelets/µL (reference range, 175,000-500,000/µL). Seven days later, a recheck CBC, serum chemistry profile, and PCR testing for infectious and tick-borne diseases revealed 1200 WBCs (reference range, 5500-16,900/µL), 140,000 platelets/µL (reference range, 175,000-500,000/µL), 60 neutrophils/µL (reference range, 2000-12,000/µL), and a sodium concentration of 136 mEq/L (reference range, 139-154 mEq/L). Henderson received lactated Ringer’s solution (500 mL SC) and was prescribed at-home medications, including enrofloxacin (10 mg/kg PO every 24 hours) and doxycycline (5 mg/kg PO every 12 hours). Results from a CBC performed 5 days later showed normal neutrophil and platelet counts; thus, antibiotics were discontinued.

Based on Henderson’s clinical course and response to antibiotic therapy alone, Rylie’s prednisone dose was tapered then discontinued, as fenbendazole toxicity was considered the likely cause of clinical illness in both dogs (see Take-Home Messages). One week after completing antibiotic treatment, Rylie’s CBC with pathologist review showed 12,580 neutrophils/µL (reference range, 2000-12,000/µL) and 447,000 platelets/µL (reference range, 175,000-500,000/µL).

Hematocrit was 44% (reference range, 39%-55%) with occasional toxic changes, occasional acanthocytes, and 1+ poikilocytes.

TAKE-HOME MESSAGES

- Bone marrow cells are susceptible to drug toxicity, as they divide rapidly and are metabolically active. Drug toxicity should always be considered a differential diagnosis for patients with generalized bone marrow hypoplasia/aplasia.
- Benzimidazoles bind to tubulin, a structural protein of microtubules, and can adversely affect rapidly dividing cells.
- Bone marrow toxicity has been reported with albendazole use in cats and dogs; however, few case reports of bone marrow toxicity after fenbendazole administration exist.
- The labeled fenbendazole dose for dogs is 50 mg/kg PO every 24 hours with food for 3 consecutive days. Extended courses of up to 14 days are generally used to treat certain parasites (eg, lungworms).
- Rylie’s presumptive generalized bone marrow hypoplasia/aplasia could have been an idiosyncratic reaction unrelated to the pharmacologic action of fenbendazole. However, because another dog in the household experienced the same clinical course following similar dosing, both dogs’ signs were likely dose dependent.

References
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*Against L. grippotyphosa

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In patients with immune-mediated diseases, identification of a possible underlying cause is critical, as remission can be harder to achieve and relapse may be more likely if an underlying cause is present but not identified. Initial diagnostic testing should be conducted before therapy, particularly with glucocorticoids, is initiated so as not to obscure the diagnosis of any secondary underlying disease (eg, lymphoma).

Glucocorticoids are usually the initial drugs of choice; secondary medications can be added in the case of severe or life-threatening disease, when adverse effects from steroids are severe, or when steroid therapy is not effective in establishing or maintaining remission. The addition of a second immunosuppressive drug has its disadvantages, though, as these drugs may be costly, have adverse effects, and may necessitate drug monitoring. Cats tend to respond well to sole steroid therapy and experience fewer adverse effects as compared with dogs. Clinical response to glucocorticoids usually appears within 3 to 7 days of initiating therapy. Patients should be monitored for secondary infections during therapy.

Other immunosuppressive drugs include azathioprine, cyclosporine, and mycophenolate mofetil. Azathioprine causes T- and B-cell suppression. In dogs, azathioprine can cause GI adverse effects, myelosuppression, hepatotoxicity, pancreatitis, and secondary infections; azathioprine is not recommended in cats due to myelosuppression. Cyclosporine is a T-cell inhibitor and blocks cytokines; adverse effects include GI upset, gingival hyperplasia, and secondary infections. Oral bioavailability of this drug can vary widely among patients; testing can be performed to ensure an adequate dose is being administered. Mycophenolate mofetil inhibits cell-mediated and humoral immune responses; most notable adverse effects are related to the GI system.

Remission should be achieved for at least 2 to 3 weeks before medication is tapered, which involves tapering one medication by 25% every 2 to 4 weeks. The medication that causes the most adverse effects (often glucocorticoids in dogs) or has the highest cost is usually tapered first. The weaning process requires 4 to 6 months; if weaning is undertaken too quickly, relapse can occur.—Archer T
Maximizing Careers for Relief Veterinarians

Being a relief veterinarian offers the flexibility to create a schedule based on one’s lifestyle and budget needs and the opportunity to work at a variety of different practices, which can help facilitate connections with multiple veterinary teams. Flexibility is a key skill needed in addition to routine veterinary expertise. Relief veterinarians should have excellent interpersonal communication skills and project both confidence and humility. Reliability and the ability to create meticulous medical records are paramount.

Those considering starting relief work should consult with their lawyer and accountant to decide the best way to proceed with regard to local laws, tax advantages, risk tolerance, and liability exposure. From a tax perspective, most relief veterinarians will be considered either an independent contractor or a relief employee. Expenses to track include equipment purchases, association dues, professional fees, continuing education, and travel costs. Insurance categories to consider include professional liability, disability, health, workers’ compensation, and, potentially, business property insurance.

Relief veterinarians can market themselves by contacting practices, using lists maintained by state associations, attending local and national meetings, joining social media groups, and using staffing agencies. Fees can be determined by using the average rate in the area; a more specific approach is to determine one’s life and business expenses and goals regarding scheduling and calculate how much to charge based on these numbers. Contracts should include these fees, services provided, species examined, schedules, and cancellation policies.—Trice CE

Managing Collapsing Trachea: Beyond Hydrocodone

Medical management of canine tracheal collapse can have variable success. Lower airway disease and other concurrent or complicating factors make development of a standard therapy difficult; thus, treatment should be determined based on the individual patient’s needs.

History, diagnostic testing, and response to therapy can all provide important insight into the best approach to treatment. Severity and location of the collapse can influence the history and clinical signs. Questions about the patient’s environment and potential coughing triggers—including cigarette smoke, floor cleaners, and fragrances—are an important part of history-taking.

Clinicians should simultaneously auscultate the patient and observe the pattern of breathing for signs of the source of disease. Extrathoracic tracheal disorders tend to cause inspiratory effort and possible stridor, whereas intrathoracic tracheal disorders and lower airway disease can lead to increased expiratory effort.

Patients with acute respiratory distress often require treatment prior to diagnostic testing. Acute interventions include oxygen therapy, obtaining vascular access, cooling measures, sedatives, and corticosteroids as indicated. Intubation or emergency tracheostomy may be required in cases of complete obstruction. Thoracic radiography is indicated in all coughing patients with signs of upper airway disease. In addition, a minimum database (ie, CBC, serum chemistry profile, urinalysis) can be helpful in evaluating overall health prior to undergoing anesthesia. Although fluoroscopy can be helpful, tracheobronchoscopy is thought to be the best diagnostic modality, as it allows for direct airway assessment down to the bronchi as well as sample collection.

Chronic management measures can include weight loss, harness use, allergen elimination, activity restriction, antitussives, bronchodilators, corticosteroids, antibiotics, anxiolytics, and lifestyle changes. Patients refractory to medical management may require intraluminal tracheal stenting.—Archer T

Intubation or emergency tracheostomy may be required in cases of complete obstruction.
Surgical Extractions: Numb It & Remove It

Tooth extractions can be challenging, particularly when the tooth is solidly fixed, has multiple roots, or is a canine tooth. Techniques for extraction include periodontal flap elevation and suturing, alveolar bone removal, crown sectioning, and alveoloplasty.

The maxillary fourth premolar has 3 roots and requires periodontal flaps for removal and use of vertical incisions that follow the lines of the tooth. When the mesial incision is advanced dorsally, the infraorbital foramen with its exiting artery and nerve should be avoided. Once the flap is completed, alveolar bone from the buccal aspect of the distal and mesiobuccal roots can be removed with a bur. Slots for later placement of the periosteal elevator may also be bored in the roots during this process. The crown should be sectioned into its root segments using the buccal and mesial furcation entrances as landmarks. The segments should be luxated in a buccal direction. Sharp, bony edges can be smoothed with the bur and the periodontal flap sutured in place. The mandibular first premolar can be removed in a similar fashion, although the buccal bone to be removed is thicker.

The maxillary canine has one root running dorsally and distally, with its apex directly above the mesial root of the maxillary second premolar. When the maxillary canine root is elevated, care should be taken to avoid fracturing the root apex, which can break through the nasal cavity. Should this occur, primary wound closure can be performed with a periodontal flap over the alveolus. A buccal approach has been recommended for removal of the mandibular canine; however, considering the structures adjacent to the mandibular canine root (eg, neurovascular structures exiting the mental foramen) and the root’s lingual direction, a lingual approach has been developed with a periosteal flap based on the symphyseal surface near the mandibular symphysis and the apex, including the gingiva of the lingual aspect of the tooth.—Smith MM

Care should be taken to avoid fracturing the root apex.

What Goes Up Must Come Down: Diagnosis & Management of Glaucoma

Glaucoma is the elevation of intraocular pressure (IOP) due to abnormal outflow of aqueous humor. Primary glaucoma is the result of a hereditary defect in the iridocorneal drainage angle and is seen in almost every dog breed but most frequently in spaniels, terriers, poodles, beagles, Labrador retrievers, chow chows, basset hounds, dalmatians, and Arctic breeds. Secondary glaucoma occurs from an inciting cause such as inflammation, lens luxation, trauma, or intraocular neoplasia. In cats, glaucoma is rare and is usually secondary, although a predisposition has been observed in several breeds (eg, Siamese, Burmese).

Glaucoma is diagnosed when IOP is >20 mm Hg in dogs and >25 mm Hg in cats and supportive clinical signs (eg, vision loss, episcleral injection, buphthalmia, pain) are observed. Ophthalmoscopy findings can include cupping or flattening of the optic disc, retinal hemorrhage or edema, and tapetal hyperreflectivity. In dogs predisposed to glaucoma, a narrowed or dysplastic filtration angle may be seen on gonioscopy.

The goal of treating glaucoma is to maintain a normal IOP and preserve vision. Subtle IOP reductions (≥5-7 mm Hg) can be achieved with β blockers (eg, timolol 0.5%); more moderate reductions (≥20%-30%) can be achieved with carbonic anhydrase inhibitors (eg, dorzolamide 2%). Both work by decreasing aqueous humor production. Prostaglandin analogs (eg, latanoprost) increase aqueous outflow and can be used in emergencies but are contraindicated in patients with secondary glaucoma. When primary glaucoma is diagnosed, prophylactic treatment should be initiated in the opposite eye. Surgical options for refractory glaucoma include a goniom implant (typically a valved shunt) or laser cyclophotocoagulation, which destroys ciliary body production of aqueous humor. Success rates for both are variable. Once vision is lost, salvage procedures include enucleation, evisceration, and/or pharmacologic ablation of the ciliary body by intravitreal gentamicin injection.—Beale B
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Optimal glycemic control requires appropriate insulin therapy to control hyperglycemia and avoid hypoglycemia and other complications. Various laboratory tests and clinical tools are available and appropriate for monitoring; however, no single method or combination has been shown to have clear, significant clinical benefits. Therefore, the monitoring program should be practical and the components tailored to meet individual patient needs and owner abilities, circumstances, and treatment goals. Recommendations for DM monitoring in dogs and cats are typically based on expert advice and experience, and published consensus guidelines are available. Elimination of clinical signs of DM is an acceptable and achievable goal for most patients, but various monitoring strategies can be used to achieve
**TABLE 1**

### DIABETES MELLITUS MONITORING METHODS

<table>
<thead>
<tr>
<th>Method</th>
<th>Monitoring Test/Procedure</th>
<th>Information Provided</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direct</td>
<td>BG curve, IGM, Spot BG determination</td>
<td>Quantitative BG concentration</td>
</tr>
<tr>
<td>Objective indirect</td>
<td>HbA1c, Serum fructosamine, Urine glucose measurement</td>
<td>Retrospective information about BG concentration</td>
</tr>
<tr>
<td>Subjective indirect</td>
<td>Clinical signs, Physical examination</td>
<td>Glycemic control inferred from history and physical examination</td>
</tr>
</tbody>
</table>

**BENEFITS OF MONITORING FOR CLINICAL SIGNS**

The usefulness of monitoring for clinical signs caused by hyperglycemia is 2-fold:

- A significant disturbance in BG can be inferred from the persistence or emergence of clinical signs during treatment (the renal threshold for glucose is ≈200 mg/dL in dogs and ≈250 mg/dL in cats).<sup>5</sup>
- Evidence shows a positive correlation between objective measures (ie, serum fructosamine and mean 8-hour BG concentration) and owner assessment of control based on clinical signs.<sup>25</sup>

Careful, frequent evaluation of clinical signs is an important part of monitoring BG and protecting overall health.<sup>25</sup> DM is a primary cause of cataracts in dogs and a cause of peripheral neuropathy in dogs and cats.<sup>26,27</sup> Thus, signs of these conditions and other common diabetic complications or concurrent disorders (eg, pancreatitis, renal failure, endocrinopathy, neoplasia) should be included in monitoring.<sup>26-28</sup>

Acceptable glycemia. Interventions should be performed frequently enough to be effective but not so often that they are impractical or inconvenient for the owner.

**Monitoring Methods**

Monitoring DM involves several direct and indirect methods for assessing glycemic control (**Table 1**). Direct monitoring uses a quantitative method to determine blood glucose (BG; eg, spot or random BG sampling, BG curve, interstitial glucose monitoring [IGM]). Indirect monitoring evaluates a subjective (eg, physical examination findings, clinical signs) or objective (eg, quantitative measurements of hemoglobin A1c [HbA1c] or fructosamine) parameter influenced by BG rather than glucose itself. Monitoring for the typical DM patient should incorporate several methods, each with advantages and disadvantages (**Table 2**).

**Assessment of Clinical Signs**

Polydipsia and polyuria are commonly observed clinical signs of DM that are directly related to the magnitude of hyperglycemia but are of limited sensitivity and specificity. Hyperglycemia results in plasma hypertonicity, which stimulates thirst and promotes volume loss via osmotic diuresis and glucosuria once the renal threshold for glucose reabsorption is exceeded.

Appetite, body weight, and body condition can also provide clues to glycemic control. Appetite persists in most diabetic dogs and cats, but body weight and condition are abnormal in many patients at the time of diagnosis; they may be improved through insulin therapy and glycemic control. Poor glycemic control should be suspected if a patient’s weight/condition does not improve or begins to decline during therapy. The monitoring strategy must detect deviations from a patient’s normal condition (see **Benefits of Monitoring for Clinical Signs**). Owners should be made aware of signs of poor glycemic control and instructed to observe water consumption, voiding habits, and appetite, along with body condition, weight, and overall health. Concerning trends or indicators should be shared with the clinician.
### TABLE 2

**ADVANTAGES & DISADVANTAGES OF DIABETES MELLITUS MONITORING METHODS**

<table>
<thead>
<tr>
<th>Monitoring Method</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ASSESSMENT OF CLINICAL SIGNS</strong></td>
<td>Easy to use frequently</td>
<td>Subjective; interpretation vulnerable to bias/expectations</td>
</tr>
<tr>
<td></td>
<td>Can correlate at-home and in-clinic observations</td>
<td>Chronic, mild/moderate BG disturbances may be missed.</td>
</tr>
<tr>
<td></td>
<td>Involves owner in pet’s care</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Absence of signs associated with improved quality of life</td>
<td></td>
</tr>
<tr>
<td><strong>GLYCATED PROTEIN MEASUREMENT</strong></td>
<td>Provides time-averaged BG information</td>
<td>Information is retrospective.</td>
</tr>
<tr>
<td></td>
<td>Monitoring is periodic; requires only a single blood sample</td>
<td>Serial sampling is more helpful than a single test result.</td>
</tr>
<tr>
<td></td>
<td>Reliable commercial assays available for HbA1c and fructosamine</td>
<td>Precise target ranges/therapeutic endpoints are undefined.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Frequent testing increases cost to owners.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Patient factors/concurrent disorders influence results.</td>
</tr>
<tr>
<td>Fructosamine</td>
<td>Reflects average BG for ≈2 weeks preceding test</td>
<td>Does not reflect long-term changes in BG status</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Does not correlate well with other glycemic assessments in some patients</td>
</tr>
<tr>
<td>HbA1c</td>
<td>Small volume sample required (several drops of blood)</td>
<td>Less sensitive to short-term changes in BG</td>
</tr>
<tr>
<td></td>
<td>Reflects average BG for 70 days (cats) or 120 days (dogs) preceding test</td>
<td>Can be influenced by factors that affect Hb concentration/turnover</td>
</tr>
<tr>
<td><strong>BG MEASUREMENT</strong></td>
<td>Provides pharmacodynamic information about response to insulin</td>
<td>Normal biologic variability may have substantial impact on results.</td>
</tr>
<tr>
<td></td>
<td>Immediate, real-time measurement of BG</td>
<td>Substantial cost</td>
</tr>
<tr>
<td>BG curve</td>
<td>Traditional, familiar technique</td>
<td>Time consuming; practical considerations limit time period over which curve can be performed.</td>
</tr>
<tr>
<td></td>
<td>Uses simple, reliable technology (glucometer)</td>
<td>Requires multiple blood samples</td>
</tr>
<tr>
<td></td>
<td>Can be performed in the clinic or at home</td>
<td>May not be predictive of future insulin needs</td>
</tr>
<tr>
<td>IGM (flash or continuous)</td>
<td>Provides timely information about insulin action</td>
<td>Changes in interstitial glucose lag behind changes in BG.</td>
</tr>
<tr>
<td></td>
<td>Provides real-time and retrospective data</td>
<td>No approved veterinary IGM units; some manufacturers may not make technology/equipment available to clinicians.</td>
</tr>
<tr>
<td></td>
<td>Well tolerated; suitable for at-home use</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Daily data can be monitored/collected over several weeks.</td>
<td></td>
</tr>
<tr>
<td>Spot BG measurement (capillary or venous blood sample)</td>
<td>Useful for documenting hypoglycemia</td>
<td>Randomly timed BG measurements have little value for patient assessment or guiding therapy.</td>
</tr>
<tr>
<td><strong>URINE GLUCOSE MONITORING</strong></td>
<td>Allows for simultaneous testing for urine glucose and ketones</td>
<td>Results are semiquantitative and lag behind blood changes.</td>
</tr>
<tr>
<td></td>
<td>May be only option for home testing for some owners</td>
<td>Glucosuria does not correlate closely with BG.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Samples may be difficult to obtain for some owners.</td>
</tr>
</tbody>
</table>
Urine Monitoring
Urine testing for glucose and ketones in DM is used to detect changes in health status before clinical signs appear. Abrupt changes in the magnitude of glucosuria or emergence of ketonuria can signal a recent disruption in glycemic control, but this advantage may not be realized in practice, as outward clinical signs often precede detection of altered urine glucose or ketone concentrations in urine. In addition, urine testing can have several drawbacks (eg, difficulty in obtaining a sample for testing, leading to poor compliance). Overall, this method is not recommended for DM monitoring; it may be useful in some circumstances but must be interpreted in context of other findings.

Glycated Proteins
Proteins exposed to glucose are altered via a non-enzymatic chemical reaction. The concentration of these glycated proteins in blood increases with the circulating BG concentration. Because glycated proteins are metabolized in the same manner as nonglycated proteins, their concentration in the circulation reflects the average BG over the lifespan of the parent protein. Serum fructosamine and HbA1c are the major glycated proteins in dogs and cats; monitoring these blood concentrations can provide insight about glycemic control and response to insulin.

Fructosamine values represent the concentrations of several glycated serum proteins, but glycated albumin makes up the largest portion. In dogs and cats, fructosamine concentration is frequently used to monitor DM and is interpreted to reflect average glycemia over the previous 2 weeks, which is the approximate lifespan of serum albumin. HbA1c is a specific glycated hemoglobin moiety used extensively for monitoring glycemia in humans with DM but is used less frequently in veterinary medicine. Due to hemoglobin’s longer serum lifetime, HbA1c levels reflect average serum glucose over the erythrocyte lifespan in circulation (dogs, ≤120 days; cats, ≈70 days). Although HbA1c represents glycemia over a substantially longer time than fructosamine, acute, short-term disruptions in glycemic control affect fructosamine sooner than HbA1c (see Drawbacks of Glycated Protein Monitoring). A reduction in fructosamine and HbA1c concentrations is expected with successful insulin therapy.

Clinicians have traditionally relied on fructosamine measurement rather than other moieties partly due to the widespread commercial availability of fructosamine assays. However, recent studies have underscored the possible advantage of HbA1c for assessing glycemic control in dogs, and commercial assays are available for assessing canine and feline HbA1c.

Blood Glucose
Direct determination of BG is the gold standard for immediate and real-time assessment of glycemia. In diabetic patients, BG monitoring over time reflects pharmacodynamic actions of insulin and can provide information about onset, peak activity, and duration of action, as well as its overall effectiveness in controlling glycemia. The BG curve has been the traditional approach used to document patient insulin response, but IGM has become more commonplace. Randomly timed, single determinations of BG concentration (ie, spot measurement) have little interpretive value and are not recommended when making decisions about insulin dose.

DRAWBACKS OF GLYCATED PROTEIN MONITORING
Medical conditions that alter concentrations of the parent protein also affect the glycated versions. Fructosamine reduction occurs in nondiabetic dogs with hypoproteinemia or hypoalbuminemia and in those with hyperlipidemia and/or azotemia. Fructosamine is also reduced in cats as a consequence of increased protein turnover associated with concurrent hyperthyroidism, although it may remain within the reference range. Many of the conditions affecting fructosamine also affect HbA1c, but HbA1c concentration is also altered by anemia and other conditions that influence RBC turnover.
The Blood Glucose Curve
This method involves sampling and testing every 1 to 2 hours over a defined time (usually 12 hours but sometimes longer) to plot BG, typically using a portable glucometer. Venous or capillary blood samples from various sites (eg, small vein, ear tip, paw pad) are obtained manually using a needle or lancet. The number of points on the curve is determined by the sampling frequency. The BG curve is most often performed in clinic, but some clinicians recommend owners learn to do it at home. A review of the background, method, and interpretation of the BG curve is available.14

Interstitial Glucose Monitoring
IGM allows for measurement of glucose concentration in interstitial fluid over days to weeks.15 IGM includes both continuous and flash glucose monitoring (FGM) methods. Continuous glucose monitoring automatically displays each glucose measurement for users in real time and can integrate with insulin pump systems to adjust insulin dosing, whereas FGM displays a single value result only when the sensor is interrogated by the reader (see Interstitial Glucose Monitoring Systems). IGM provides values for glucose that differ from those of capillary or venous blood.16 The gradient between blood and interstitial glucose, which can range from 20% to 110%,16 is greatest when large fluctuations in BG (increasing or decreasing) occur and there is a lag (minutes) before the 2 compartments equilibrate. Thus, IGM may underreport rapid changes in BG, which is particularly important when there is risk for development of hypoglycemia.

Monitoring performed by pet owners is a viable way for the clinician to obtain BG information.17,18 In a study, ≈85% of owners were successful with long-term home BG monitoring that required frequent blood sampling to produce curves.19 Anecdotal reports indicate owners and clinicians are willing to use IGM to perform at-home monitoring; this is especially true when an FGM device is used, as these systems do not require frequent calibration and data can be easily retrieved and analyzed. A particular advantage of FGM systems

**INTERSTITIAL GLUCOSE MONITORING SYSTEMS**
IGM has been used in veterinary medicine for >15 years.33 Several systems studied have proven useful in dogs and cats.34 Advances in technology have rendered IGM systems more user friendly and better suited for veterinary applications. A newer FGM system has shown promise in veterinary medicine, although published information is limited to a single study.35 All commercial IGM systems involve similar components and operating principles.35 The basic unit consists of a disposable sensor that combines a serum chemical detection system with a transmitter and receiver that collect, store, and display BG data. A stylet introduces the sensor through the skin and positions the tip to contact the interstitial fluid. The body of the sensor, which contains the transmitter, is affixed to shaved skin using a mild adhesive (Figure 1).

An incorporated chemical reaction platform metabolizes interstitial glucose to generate an electrical signal that is proportional to its concentration.15 A description of the use of an FGM device in small animals is available.36

**FIGURE 1** A sensor unit from a flash device adhered to the skin of a diabetic cat. A manufacturer-provided device easily applies the small sensor unit (35-mm diameter × 5-mm height) to the shaved area. The sensor uses a flexible filament in contact with the interstitial fluid to measure BG every 60 seconds and data storage capacity to record BG data. Wireless technology transfers BG data stored in the sensor unit to a handheld reader unit.

BG = blood glucose
DM = diabetes mellitus
FGM = flash glucose monitoring
HbA1c = hemoglobin A1c
IGM = interstitial glucose monitoring
is that daily glycemic data can help facilitate treatment to achieve clinical goals rather than just elimination of clinical signs. For example, insulin treatment can be adjusted more frequently based on glycemic data and metabolic targets (eg, desired range for average daily glucose).

**Interventional vs Dose Monitoring**
When considering methods of glucose monitoring, it is worth drawing distinctions between BG monitoring performed to determine a patient’s global response to a particular dose of insulin (ie, dose monitoring) and monitoring performed to determine whether a patient’s immediate glycemic status requires correction (ie, interventional monitoring). Both can be accomplished through available techniques, have the same advantages and disadvantages, and can be used in making therapeutic decisions. In practice, however, these are very different approaches to managing glycemia (*Figure 2*).

Monitoring BG in veterinary patients generally serves to assess the larger picture of insulin response and BG control over the day rather than as a guide for day-to-day changes in therapy. Dose monitoring can be useful and provide helpful information, but the use of interventional monitoring should be considered cautiously. Although some pet owners may be interested in and eager to attempt interventional monitoring and make insulin adjustments, the author does not recommend it, as there has been little evidence to show that the effort and expense actually improve long-term outcomes or reduce complications, and the very stringent targets for BG control involve increased risk for hypoglycemic events in human and, probably,
veterinary patients. Studies addressing these concerns are limited. In a small group of cats receiving at-home monitoring to achieve tight BG control, complication rate was low, but constant care and anxiety regarding hypoglycemia are common concerns among pet owners and chronic or recurrent hypoglycemia can lead to increased patient morbidity and poor quality of life. Some clinicians use a modified approach to interventional monitoring described above by having owners check BG immediately before an insulin dose and use the information to modify the dose as necessary. An advantage of this approach is the opportunity to reduce the likelihood of hypoglycemia, but the clinician must provide the owner with clear goals and guidelines for making dose decisions.

Regardless of the method used to obtain a BG curve, comparison with other measures used to assess BG control (eg, clinical evaluation, markers of long-term glycemic control) can help validate results. The BG curve is especially helpful in detecting hypoglycemic events during testing. Hypoglycemia typically reflects an excess of insulin and should prompt dose reduction. Curve analysis can also demonstrate persistent hyperglycemia, which is consistent with poor glycemic control. Troubleshooting persistent hyperglycemia is more difficult than troubleshooting hypoglycemia, as the former can have numerous causes (eg, poor compliance, problems with insulin administration, underdosing, insulin resistance).

A major limitation of the BG curve is imposed by biologic variability that impacts day-to-day insulin action. Depending on insulin type and formulation used, absorption and activity in humans under experimental conditions can vary from 15% to 50% day to day. Variability is typically greater in clinical patients, with inconsistent or unpredictable changes in glycemia even after administration of equivalent doses of the same insulin. Numerous factors, including the patient’s emotional state (eg, stress or anxiety), exercise, body temperature, and comorbidities, among others, may contribute to variability.

The veterinary literature contains examples of the effect of biologic variability on BG curve data. In a study, dogs receiving the same insulin type and dose showed marked variability in routinely determined BG curve parameters, including minimum, maximum, and mean BG concentrations and time to nadir, on 12-hour BG curves obtained 24 hours apart. In that study, curve analysis resulted in a different insulin treatment recommendation in nearly 45% of paired curves and treatment recommendations were frequently opposite (ie, one curve of the pair indicated a need for a dose increase and the other indicated a need for a dose decrease).

**Conclusion**

No single monitoring tool or combination has been shown to provide significant, measurable advantages in diabetic dogs or cats. Reliance on a single tool is discouraged. Effective monitoring should incorporate several methods that assess different aspects of glycemic control. A flexible and practical monitoring program that aims to provide objective information while balancing patient and owner needs can engage the pet owner as a primary caregiver, enhance compliance, and strengthen the clinician–pet owner relationship.

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**References**


LOOK FOR THESE ARTICLES IN FUTURE ISSUES

- Puppy & Kitten Socialization
- Step-by-Step: Urinary Catheterization
- Case: Cryptococcosis in a Cat
- Improving Medication Compliance in Pet Owners
- Differentials List: Hypophosphatemia
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IMPORTANT SAFETY INFORMATION: BRAVECTO has not been shown to be effective for 12-weeks' duration in puppies or kittens less than 6 months of age. BRAVECTO Chew: The most common adverse reactions recorded in clinical trials were vomiting, decreased appetite, diarrhea, lethargy, polydipsia, and flatulence. BRAVECTO is not effective against lone star ticks beyond 8 weeks of dosing. BRAVECTO Topical Solution for Dogs: The most common adverse reactions recorded in clinical trials were vomiting, decreased appetite, diarrhea, lethargy, polydipsia, and flatulence. BRAVECTO is not effective against lone star ticks beyond 8 weeks of dosing. BRAVECTO Topical Solution for Cats: The most common adverse reactions recorded in clinical trials were vomiting, itching, diarrhea, hair loss, decreased appetite, lethargy, and scabs/ulcerated lesions. BRAVECTO is not effective against American dog ticks beyond 8 weeks of dosing. For topical use only. Avoid oral ingestion. The safety of BRAVECTO has not been established in breeding, pregnant and lactating cats. Use with caution in cats with a history of neurologic abnormalities. Neurologic abnormalities have been reported in cats receiving BRAVECTO, even in cats without a history of neurologic abnormalities. See full Prescribing Information on page 36.
Flavored chew for dogs.

**BRIEF SUMMARY** (For full Prescribing Information, see package insert)

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

**Indications:** Bravecto kills adult fleas and is indicated for the treatment and prevention of flea infestations (Ctenocephalides felis) and the treatment and control of tick infestations (Ixodes scapularis [black-legged tick], DermoDermacentor variabilis [American dog tick], and Rhipicephalus sanguineus [brown dog tick]) for 12 weeks in dogs and puppies 6 months of age and older, and weighing 4.4 pounds or greater.

Bravecto is also indicated for the treatment and control of Amblyomma americanum (flea star-tick) infestations for 8 weeks in dogs and puppies 6 months of age and older, and weighing 4.4 pounds or greater.

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

**Warnings:**

Not for human use. Keep the product and all drugs out of the reach of children. Do not contact or allow children to contact the application site until dry. Keep the product in the original packaging until use so that children do not get direct access to the product. Do not eat, drink or smoke while handling the product. Wash hands thoroughly with soap and water immediately after use of the product.

**Precautions:** Bravecto has not been shown to be effective for 12-weeks duration in puppies less than 6 months of age. Bravecto is not effective against Amblyomma americanum ticks beyond 8 weeks after dosing.

**Adverse Reactions:**

In a well-controlled U.S. field study, which included 224 dogs (224 dogs were administered Bravecto every 12 weeks and 70 dogs were administered an oral active control every 4 weeks and were provided with a tick collar), there were serious adverse reactions. All potential adverse reactions were recorded in dogs treated with Bravecto over a 126-day period and in dogs treated with the active control over an 84-day period. The most frequently reported adverse reaction in dogs in the Bravecto and active control groups was vomiting.

**Percentage of Dogs with Adverse Reactions in the Field Study**

<table>
<thead>
<tr>
<th>Adverse Reaction (AR)</th>
<th>Bravecto Group: Percentage of Dogs with the AR During the 182-Day Study (n=224 dogs)</th>
<th>Active Control Group: Percentage of Dogs with the AR During the 84-Day Study (n=70 dogs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vomiting</td>
<td>7.1</td>
<td>14.3</td>
</tr>
<tr>
<td>Decreased Appetite</td>
<td>6.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>4.9</td>
<td>2.9</td>
</tr>
<tr>
<td>Lethargy</td>
<td>5.4</td>
<td>7.1</td>
</tr>
<tr>
<td>Polydipsia</td>
<td>1.8</td>
<td>4.1</td>
</tr>
<tr>
<td>Alopecia</td>
<td>1.3</td>
<td>0.0</td>
</tr>
</tbody>
</table>

In a well-controlled laboratory dose confirmation study, one dog developed edema and hypoplasia of the upper lips within one hour of receiving Bravecto. The treated animal was not visibly affected during the study and had resolved with veterinary intervention by the next morning.

**For technical assistance or to report a suspected adverse drug reaction, contact Merck Animal Health at 1-800-224-5318. Additional information can be found at www.bravecto.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.**

**How Supplied:**

Bravecto is available in five strengths (112.5, 250, 500, 1000, and 1400 mg fluralaner per tube). Each tube is packaged individually in a pouch. Product may be supplied in 1 or 2 tubes per carton.

**BRAVECTO** (Fluralaner topical solution) for Cats

**BRIEF SUMMARY** (For full Prescribing Information, see package insert)

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

**Indications:** Bravecto kills adult fleas and is indicated for the treatment and prevention of flea infestations (Ctenocephalides felis) and the treatment and control of lice infestations (Dermacentor variabilis [American dog tick]) and Rhipicephalus sanguineus (brown dog tick) for 12 weeks in cats and kittens 6 months of age and older, and weighing 2.6 pounds or greater.

Bravecto is also indicated for the treatment and control of DermoDermacentor variabilis (American dog tick) infestations for 8 weeks in cats and kittens 6 months of age and older, and weighing 2.6 pounds or greater.

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

**WARNINGS**

**Human WARNINGS:**

Not for human use. Keep this and all drugs out of the reach of children. Do not contact or allow children to contact the application site until dry. Keep the product in the original packaging until use in order to prevent children from getting direct access to the product. Do not eat, drink or smoke while handling the product. Avoid contact with skin and eyes. If contact with skin or eyes occurs, flush eyes slowly and gently with water. Wash hands and contact skin thoroughly with soap and water immediately after use of the product.

**For technical assistance or to report a suspected adverse drug reaction, contact Merck Animal Health at 1-800-224-5318. Additional information can be found at www.bravecto.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.**

**How Supplied:**

Bravecto is available in three strengths for use in cats (112.5, 250, 500 mg fluralaner per tube). Each tube is packaged individually in a pouch. Product may be supplied in 1 or 2 tubes per carton.
Hyperkalemia

Julie Allen, BVMS, MS, MRCVS, DACVIM (SAIM), DACVP

Following are differential diagnoses, listed in order of likelihood,* for patients presented with hyperkalemia.

- Pseudohyperkalemia
  - Potassium EDTA contamination
  - Hemolysis (in vitro or in vivo) or RBC leakage in certain Asian breeds that have high-potassium erythrocytes (eg, Shiba Inu) or any breed with marked reticulocytosis
  - Thrombocytosis and, possibly, marked leukocytosis (eg, leukemia)
  - Contamination with high-potassium fluids due to collection from improperly flushed IV line
- Urethral (or, less likely, bilateral ureteral) obstruction
- Acute kidney injury (oliguric/anuric)
- End-stage kidney disease (oliguric/anuric)
- Uroabdomen
- Hypoadrenocorticism
- Chronic kidney disease
- Drug-induced/iatrogenic cause; usually only in combination with other issues (eg, decreased renal function). May decrease renal excretion and/or affect transcellular movement
  - ACE inhibitors (eg, enalapril)
  - Aldosterone antagonists (eg, spironolactone)
  - Angiotensin II-receptor blockers (eg, telmisartan)
  - NSAIDs
  - Cyclosporine or tacrolimus
  - Trimethoprim/sulfonamides (trimethoprim decreases potassium excretion in the distal renal tubule)
  - Trilostane
  - Mitotane

*Order of likelihood is based on the author’s personal experience.

References
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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.
Radiation Therapy & Patient Quality of Life

Andy Abbo, DVM, MS, DACVIM (Oncology)
Veterinary Cancer Specialists of New England
Buzzards Bay, Massachusetts

In the Literature

FROM THE PAGE …

The perception of a pet’s quality of life (QOL) during cancer therapy is a common concern among pet owners when making cancer treatment decisions. Radiation therapy (RT) is most commonly recommended as part of a multimodal approach to local disease control (ie, combined with surgery and/or chemotherapy). RT can be administered on a palliative basis or as a definitive protocol. Definitive protocols typically consist of 15 to 20 daily treatments, whereas palliative therapy consists of 3 to 4 weekly treatments. Acute adverse effects of definitive RT can include mucositis, leukotrichia, and localized discomfort and can generally be managed with pain and anti-inflammatory medications on an as-needed basis. Acute adverse effects typically resolve relatively quickly with supportive care. Palliative approaches are typically associated with a much lower risk for acute adverse effects and are often appealing for this reason; however, palliative approaches vary in efficacy, as they are designed to provide comfort and slow progression of disease. Palliative RT typically does not lead to long-term disease control.

This study sought to determine owners’ perceptions of their dog’s QOL during and after RT. Seventy-one owners were surveyed about their feelings and experiences with regard to their dog’s RT. Results found that 92% of respondents were happy they had chosen to treat their pet with RT; 88% reported they would consider RT in another pet if it were indicated. Across all time points (ie, prior to RT, on the last day of RT, >6 weeks after RT), owner-reported QOL scores were consistently high; owner satisfaction with the decision to pursue RT was independent of the protocol chosen. When palliative care was evaluated separately, however, QOL scores 6 weeks after completion of RT were lower than scores given before treatment. Because acute adverse effects are not generally seen with palliative approaches, this lower scoring may be attributed to possible earlier disease progression with palliative approaches.

… TO YOUR PATIENTS
Key pearls to put into practice:

1. Most owners who choose to pursue RT are happy with their decision. Although adverse effects can occur, these tend to be manageable and do not significantly affect a pet’s QOL during therapy.

2. Owner education is critical. RT requires significant time and financial commitment. Definitive RT is most commonly used for incompletely or marginally excised disease (eg, soft tissue sarcoma, anal sac adenocarcinoma, mast cell tumor). Because RT is only useful for local disease control, staging prior to RT is recommended. Palliative therapy may be used for any tumor with limited risk for acute adverse effects; however, the goal of this approach is to provide comfort, and efficacy is variable.

3. Referral to an oncologist is recommended to discuss the pros and cons of each approach, as well as the expectations of therapy.
Research Note: 
Relationship Between Breed & Hemivertebrae

Hemivertebrae are the most common vertebral body malformations in screw-tailed brachycephalic breeds. Although hemivertebrae are incidental findings in many instances, they can also cause spinal cord dysfunction, particularly in pugs. This study compared different hemivertebra subtypes among these breeds. Hemivertebrae were classified into subtypes, and the associated spinal curvature was quantified using Cobb angle measurements. Certain breeds were found to be more associated with certain hemivertebra subtypes. In addition, the ventral hypoplasia subtype was found to be associated with higher Cobb angles and a higher likelihood of kyphosis. The ventral hypoplasia subtype was the most common subtype in pugs, which was the only breed found to have this subtype. Although the clinical significance of these findings is unknown, the authors suggest these findings may explain why pugs appear to be more predisposed to development of clinical signs attributed to hemivertebrae as compared with other screw-tailed brachycephalic breeds.

Source
Potential Adjunct Therapy for Allergic Cats

William Oldenhoff, DVM, DACVD
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Madison, Wisconsin

In the Literature

FROM THE PAGE …

Few options are available for the treatment of feline allergic dermatitis; this may be due to the fact that feline hypersensitivity dermatitis is generally less understood as compared with its canine counterpart, atopic dermatitis. Palmitoylethanolamide (PEA) is a lipid compound that has anti-inflammatory effects and acts by down-regulating many of the cells involved in the allergic response (eg, cutaneous mast cells, T cells, keratinocytes, macrophages). This study* investigated the use of ultramicronized PEA (PEA-um) in cats with non-flea–hypersensitivity dermatitis.

Fifty-seven cats were initially enrolled in this double-blind study, but only 25 met all requirements for analysis. Cats received a 28-day tapering course of methylprednisolone and were assigned to either the PEA-um group or the placebo group; PEA-um (15 mg/kg PO every 24 hours) or placebo was administered for 12 weeks. Cats were assessed throughout the study through the use of an owner-reported visual analog scale and global assessment score, as well as a clinician-reported validated score for assessment of skin lesion extent and severity. Cats receiving PEA-um had lower pruritus scores as compared with placebo-treated cats both when steroids were stopped and when a flare was noted following steroid cessation. In addition, cats that received PEA-um had a significantly longer time until relapse following steroid cessation (mean, 40.5 days as compared with 22.2 days in the placebo group). In the PEA-um group, 33% of owners reported that there was no worsening of their cat’s condition following steroid discontinuation, an observation not noted by any owners of placebo-treated cats.

… TO YOUR PATIENTS

Key pearls to put into practice:

1. Allergy management requires a multimodal approach. No single treatment will work perfectly for all allergic patients. There are fewer therapeutic options available for cats, so new options are needed. PEA-um is a promising potential tool for allergy management in cats.

2. PEA-um should be used primarily as an adjunct therapy to other treatments. This study suggests that PEA-um has a steroid-sparing effect; however, further research is needed.

3. PEA-um is available in the United States as a soft chew for dogs. This study used a liquid form, which is not commercially available in the United States.

*This study was funded by Innovet Italia Srl.
The Effect of Shock on Tissue Oxygen Levels in Dogs

Selena L. Lane, DVM, DACVECC
University of Georgia

In the Literature

FROM THE PAGE …

Shock is a life-threatening condition that can occur secondary to various clinical conditions and results in decreased oxygen delivery to tissue. Near-infrared spectroscopy is a noninvasive diagnostic tool that has been investigated as a means to continuously measure tissue oxygen saturation (StO2), which can be a marker of oxygen delivery to tissue and useful in the diagnosis of shock. It is unknown whether StO2 measurements reflect shock in dogs presented emergently or whether alterations in StO2 are associated with illness severity or mortality.

This prospective, clinical study performed over 4 years in a veterinary teaching hospital evaluated 25 dogs with naturally occurring shock, excluding cardiogenic shock. Data collected on each dog, including peripheral oxygen saturation, blood pressure, lactate levels, and blood gas analysis, were used to calculate the Acute Patient Physiologic and Laboratory Evaluation (APPLE) score to stratify illness severity. Higher APPLE scores are associated with higher illness severity. StO2 measurements were obtained before any treatments were administered.

Of the dogs enrolled, mean StO2 was 65.12% (±17.7%) and ranged from 23% to 92%. Hyperlactatemia was common in this patient population. A low StO2 was moderately correlated with increased APPLE scores, and single StO2 measurements were not predictive of mortality. The APPLE score, calculated based on physical examination, laboratory, and diagnostic test findings, was the only factor in this particular study that was predictive of whether a patient would survive.

Dogs emergently presented in shock will have low StO2 values, which is consistent with expected poor oxygen delivery to tissue during shock. Low StO2 is associated with more severe disease, but a single StO2 measurement may not be helpful in predicting whether a patient will survive. Calculating the APPLE score to identify the sickest patients may be useful when providing prognostic information to owners. Although measuring StO2 is quick and noninvasive, the clinical utility of StO2 is limited, as the equipment is not readily available in most clinics and further information is needed to determine how StO2 levels relate to patient outcomes over time.

… TO YOUR PATIENTS
Key pearls to put into practice:

1. StO2 can be used as an adjunctive measure of disease severity in patients with shock.
2. Illness severity scores (eg, APPLE score) can be used to provide prognostic information for owners of critically ill dogs in shock.
3. Stabilization of dogs in shock should focus on optimizing tissue perfusion and oxygen delivery to ensure the best outcome for the patient.

Suggested Reading
Minocycline as an Alternative to Doxycycline in the Treatment of Canine Heartworm Disease

C. Thomas Nelson, DVM*

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Companion Animal Practices of North America
Anniston, Alabama

In the Literature

FROM THE PAGE ...

The shortage and subsequent increase in cost of doxycycline have led to a search for alternative antibiotics and dose protocols. This study sought to determine whether minocycline is an effective alternative to doxycycline and whether a lower dose of doxycycline is as effective as the American Heartworm Society recommended dose in eliminating *Wolbachia* spp from *Dirofilaria immitis* microfilariae. Minocycline has been shown to be more effective in eliminating *Wolbachia* spp from the filarial nematode *Onchocerca gutturosa* as compared with doxycycline, and minocycline at 5 mg/kg every 12 hours has been suggested to be as effective as doxycycline based on pharmacokinetic/pharmacodynamic analysis of a mouse model.

Thirty-two dogs naturally infected with heartworms received either doxycycline or minocycline at 5 mg/kg or 10 mg/kg every 12 hours for 28 days (n = 8 per group). Microfilariae were analyzed for the presence of *Wolbachia* spp DNA using quantitative PCR testing, and adverse GI effects were documented. All microfilariae from dogs treated with doxycycline at 10 mg/kg every 12 hours were negative for *Wolbachia* spp by day 28. Two dogs in the 5 mg/kg doxycycline group, 2 in the 10 mg/kg minocycline group, and 3 in the 5 mg/kg minocycline group remained positive for *Wolbachia* spp after 28 days. GI signs (eg, vomiting, diarrhea) occurred more commonly in both the 10 mg/kg doxycycline and minocycline groups, although more dogs in the minocycline group experienced these effects.

The American Heartworm Society recommends administering a macrocyclic lactone heartworm preventive and doxycycline at 10 mg/kg every 12 hours for 4 weeks prior to administration of the adulticide melarsomine. The purpose of this pretreatment phase is to eliminate the obligate endosymbiont *Wolbachia* spp. *Wolbachia* spp and its associated surface proteins (WSP) have been implicated in the pathogenesis of filarial disease. It should be noted that this article states that the recommended dose and duration were extrapolated from the treatment of other rickettsial infections; although this was a consideration, data from additional studies contributed to the recommendations. One study reported that a 25-day course of tetracycline administration was more effective than a 15-day course for suppressing microfilaremia in the filarial nematode *Brugia pahangi*. Another study reported that doxycycline at 20 mg/kg every 24 hours for 30 days was highly effective in the elimination of *Wolbachia* spp from *D immitis* based on PCR analysis. Additional data showed reduced antibodies against WSP and IL-8 levels with a doxycycline dose of 10 mg/kg every 24 hours but no apparent

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*C. Thomas Nelson is the immediate past president of the American Heartworm Society and is affiliated with Ceva Animal Health.*
radiographic improvement in the lungs, suggesting 20 mg/kg every 24 hours may result in a significant decrease in Wolbachia spp inflammatory-mediated reactions. The same author later reported this higher dose reduced lesion scores in a study. However, the optimum dose and duration of treatment have yet to be determined.

... TO YOUR PATIENTS

Key pearls to put into practice:

1. Doxycycline at 10 mg/kg every 12 hours for 28 days appears to be the most effective treatment in eliminating Wolbachia spp, which have been shown to contribute to pulmonary arterial and parenchymal lesions.

2. Administering doxycycline with food may help reduce GI effects without significantly reducing drug absorption.

3. If vomiting or diarrhea is a significant problem, the dose of doxycycline may be reduced to 5 mg/kg every 12 hours.

References


Environmental Considerations for Snakes

Adolf K. Maas III, DVM, DABVP  
(Reptile & Amphibian Practice), CertAquV  
ZooVet Consulting  
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In the Literature

FROM THE PAGE …

Animal welfare encompasses the idea that not only basic needs be provided for an animal but also the care and materials necessary for improved quality of life. Although animal welfare has traditionally focused on domestic animals, it now focuses on animals in research environments as well. Subsequently, welfare practices for exotic and nontraditional species (eg, birds, exotic pets, primates, megavertebrates) have been developed. Zoos are now exceptionally cognizant of the role of improved welfare in the care of their animals.1

Although reptiles have generally been included in considerations of welfare and husbandry standards, for snakes, little scientific assessment of the environment necessary for improved quality of life has been performed other than in the basic needs of heat and diet. Whereas specialized lighting, furniture, enrichment, and cage supplementation are all common husbandry considerations for pet chelonia and lizards, husbandry for captive snakes in private collections often includes little more than heat, a water source, and bedding.

This research article examined the commonly maintained perception that snakes do not require space or environmental enrichment.2 Daytime observations of 31 species of snakes were held in 8 zoologic institutions in which the snakes were housed in enclosures allowing them to display a variety of behaviors as well as extend their full body length. It was found that 47% of the species observed adopted straight line or near straight line/stretched positioning, challenging the traditional belief that snakes do not require space and/or mental stimulation in their enclosure. These results provide an early step in the process of determining the needs of these complex species and critical information to build on.

Clinicians practicing serpentine medicine, however, can readily use this information. Health issues related to husbandry are common in captive snakes, and many of the issues listed in this article (eg, obesity, heart disease, sepsis, arthritis) are among the most commonly seen in practice.3 Many are resolvable by optimizing environments, thus providing opportunities for clinicians to improve their ability to evaluate the patient.
Providing structure and an environment that appropriately enriches a captive snake is as necessary for these species as it is for any other species.

**References**

Hemophagocytosis in Cats

Anne Barger, DVM, MS, DACVP
University of Illinois

In the Literature

FROM THE PAGE …

Hemophagocytosis is the macrophage phagocytosis of blood cells, including erythrocytes, leukocytes, platelets, and their precursors. Depending on the cell type phagocytized, hemophagocytosis can be further described as erythrophagia (ie, phagocytosis of RBCs) or leukophagia (ie, phagocytosis of WBCs). Hemophagocytosis can occur as a way to eliminate old and dying cells or, in the case of erythrophagia, may indicate hemorrhage. In some cases, however, the presence of hemophagia in the absence of hemorrhage or aging cells raises concern for a more severe underlying disease process (eg, neoplasia, immune-mediated disease, significant inflammation). There have only been a few reports of inappropriate hemophagocytosis in cats1,2; therefore, identification of erythrophagia, particularly in the absence of obvious hemorrhage, is concerning.

Hemophagocytic syndrome—referred to in humans as hemophagocytic lymphohistiocytosis—is a rare disease that can be familial or acquired.3 This syndrome is the result of overreactive T cells, macrophages,

▲ FIGURE Cytospin preparation of a hemorrhagic effusion from a dog. Erythrophagia (one represented by the arrow) can be noted in several macrophages.
and other histiocytic cells and can result in peripheral cytopenias. In humans, it has been reported to accompany various infectious organisms, including viruses, *Toxoplasma gondii*, and *Cryptococcus* spp; in such cases, patients are frequently immunosuppressed.4

In the present case series report, the authors describe 32 cats infected with *Histoplasma* spp-like organisms that had accompanying hemophagia noted on cytology. Many of these cats also had concurrent cytopenias, which may or may not have been the result of hemophagocytosis. This is an important sequela to consider if a patient has cytopenia associated with an infectious disease that does not correct when the infection is appropriately treated. Erythrophagia has been reported previously in cats with neoplasia and immune-mediated disease but has not commonly been reported to be associated with an infectious organism. In the single case report of feline hemophagocytic syndrome identified in the literature, the cat was FIV positive.2 These results suggest that fungal infection may be another important differential if hemophagia is noted on cytology or histopathology.

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... TO YOUR PATIENTS

Key pearls to put into practice:

1. Hemophagia is a nonspecific pathologic finding associated with inflammation or hemorrhage or may be indicative of underlying immune-mediated, infectious, or neoplastic disease.

2. Systemic fungal disease should be considered as a differential when hemophagia is noted on a feline cytologic sample.

References

Research Note: 
**Canine Cytochrome B Blood Mutations**

Mutations in *Babesia gibsoni* mitochondrial cytochrome b genes—specifically at the M128 position—are associated with resistance to atovaquone, which can lead to treatment failure. This study sought to determine M128 mutation prevalence in *B. gibsoni* in blood from dogs in North America. The study also evaluated how many of these patients had wild-type cytochrome b in initial blood samples and M128 mutations in follow-up samples. Prevalence of the M128 mutation in the 173 dogs tested was 3.5%; incidence of new cytochrome b mutations in the 43 dogs with follow-up testing was 12.1%. American Staffordshire/American pit bull terriers comprised 74% of dogs infected with *B. gibsoni* in this study. The authors concluded that the cytochrome b mutation is not common enough to warrant pretreatment mutation screening prior to therapy.

**Source**

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Research Note: 
**Feline Diffuse Iris Melanoma: A Diagnostic Dilemma**

Feline diffuse iris melanoma (FDIM) accounts for ≈50% of feline intraocular neoplasms and has a metastatic rate of 19% to 63%. Differential diagnoses include iris nevi, melanosis, and iridociliary cysts. FDIM, however, can only be diagnosed via histopathology, and because eyes in FDIM patients often remain visual, ophthalmologists may have to choose between enucleating an eye that may be healthy or monitoring a lesion that may metastasize. Circulating free nucleic acid (ie, cell-free DNA) has been shown to have potential diagnostic and prognostic value in some neoplastic diseases in dogs and humans. However, this study found no significant differences in cell-free DNA concentration and integrity among the FDIM, iris nevi, and control groups.

**Source**
Achieving pet owner compliance with veterinarian-recommended flea and tick prevention can be difficult. Owners may be reluctant to treat all household pets, particularly those the owner perceives as low risk for infestation. A recent study found owners who do purchase flea and tick preventives often do not adhere to the recommended duration of protection.1

Owners need to obtain a preventive product and using a product that is easier to administer may help owners achieve a better rate of compliance.1 Less frequent administration of flea and tick preventives may make it easier for owners to meet veterinary recommendations to treat all household pets, rather than restricting treatment to just one or two pets.

A recent study showed that dog owners who obtained a flea and tick preventive with a longer-acting duration (ie, 12 weeks) purchased more flea and tick preventives in a year than those who obtained shorter-acting duration (ie, 1 month) preventives.2 Pet owners report higher satisfaction with and preference for a flea and tick preventive with 12-week dosing intervals as compared with a preventive with 1-month dosing intervals.4 Moreover, a recent study found a single topical dose of a 12-week product provided excellent flea control in cats, achieving >96% reduction in flea counts within 7 days and 100% at 12 weeks posttreatment.5

Conclusion
Best medicine practices include making the best recommendations to veterinary patient owners. The combination of easier, less frequent dosing of flea and tick preventives increases the likelihood pet owners will comply with veterinarian recommendations.

Addressing the Challenges of Owner Compliance

Educating owners on infestation risks (eg, dermatologic, infectious, zoonotic diseases) can help owners understand the need for prevention.

It is key that owners understand effective control of fleas and ticks requires treatment of all dogs and cats in the house, and that treatment is not contingent on the amount of time a pet spends outdoors, as infestation can be spread from other pets in the household, free-roaming dogs and cats, and some urban wildlife. Owners should also understand the duration of treatment is critical, and that a preventive should also halt the flea life cycle.2 A single dose of a 3-month product has been shown to eliminate flea infestation, but a single dose of a 1-month product does not.3

Simplifying flea and tick prevention (ie, decreasing the frequency in which owners need to obtain a preventive product and using a product that is easier to administer) may help owners achieve a better rate of compliance.1 Less frequent administration of flea and tick preventives may make it easier for owners to meet veterinary recommendation to treat all household pets, rather than restricting treatment to just one or two pets.

A recent study showed that dog owners who obtained a flea and tick preventive with a longer-acting duration (ie, 12 weeks) purchased more flea and tick preventives in a year than those who obtained shorter-acting duration (ie, 1 month) preventives.2 Pet owners report higher satisfaction with and preference for a flea and tick preventive with 12-week dosing intervals as compared with a preventive with 1-month dosing intervals.4 Moreover, a recent study found a single topical dose of a 12-week product provided excellent flea control in cats, achieving >96% reduction in flea counts within 7 days and 100% at 12 weeks posttreatment.5

REFERENCES

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VALIDITY OF BEHAVIOR EVALUATIONS FOR SHELTER DOGS

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IN THE LITERATURE

FROM THE PAGE …

Canine behavior evaluations are performed in shelters ostensibly to determine a dog’s suitability for adoption. Evaluations typically consist of subtests in which the evaluator observes the dog’s responses to assess various behavior traits (eg, evaluating sociability and aggression when the dog is being pet, being restrained, approaching another dog, or responding to removal of a toy). Several published behavior evaluation protocols exist,1,2 but no standard test has been established. Individual shelters may choose which, if any, evaluation to use, with some shelters modifying existing protocols or developing their own. Despite widespread use of behavior evaluations and numerous scientific studies, there continues to be confusion surrounding the validity of these tests and whether they can accurately predict future aggressive behavior. This confusion is concerning, as the results of these tests may be used to make life-or-death decisions for many shelter dogs and can impact public health and safety.

The authors of this study searched online databases to determine the extent of the reported reliability, validity, and predictive ability of canine behavior assessments in previous studies. Seventeen studies from 8 countries were identified. The authors found that most studies did not report criteria necessary to meet the scientific standard of test validation, namely reliability (ie, reproducible measurements) and construct validity (ie, how strongly an evaluation measures what it claims to be measuring).

Predictive ability (ie, the likelihood of the assessment predicting the behavior of an individual dog in real life) is determined by the sensitivity and specificity of the assessment and is affected by the prevalence of behaviors in the general population. Sensitivity, specificity, false-positive rates, and false-negative rates were reported or calculated from the 8 studies for one or more behaviors, and all were found to have widely varying ranges; this led the authors to conclude that no canine behavior assessment or subtest has sufficient evidence to be considered a reliable test in shelters.
Five reasons were attributed to the discrepancy between the actual existence of validated evaluations that can reliably predict behavior and what clinicians believe has already been proven through research studies:

- Confusion resulting from mixing colloquial and scientific use of words (eg, validated, predictive, reliable, agreement)
- Erroneous interchangeable use of the terms “correlation” and “agreement” and the limitations of correlation and regression as statistical methods for demonstrating agreement or predictive ability
- The difference between predictive validity of an assessment used under research conditions versus the predictive ability of an assessment to accurately predict individual dog behavior in the real world
- Conflating statistical significance with clinical significance when interpreting results of behavior evaluations
- Presenting studies as validated despite actual results being less determinate

… TO YOUR PATIENTS

Key pearls to put into practice:

1. Behavior assessments are not a valid or reliable predictor of aggression after adoption. Euthanasia decisions should not be based solely on a dog’s performance in a behavior assessment.

2. Information used to understand and evaluate a dog’s behavior should come from and be corroborated by multiple sources and should include information provided by the previous owner and/or foster caretaker, as well as shelter staff observing the dog engaging in activities that would occur in a home (eg, walks, play, socialization).

3. Shelters vary in how they obtain behavior information, how or whether they use behavior assessments, and how they determine suitability for adoption. Local shelters should be contacted to inquire about their policies.

References

Suggested Reading
GI signs are a common presentation in dogs and cats. Increased availability of diagnostics can improve the quality of care for veterinary patients with GI disease but can also present a diagnostic challenge to veterinarians when choosing appropriate tests and interpreting results. This quiz will help address frequent misconceptions about some of the most commonly used GI diagnostic tests.

**QUESTION 1**
A 2-year-old neutered male crossbreed dog *(Figure)* is presented for polyphagia, severe weight loss, and chronic diarrhea.

The most sensitive and specific test for diagnosis of canine exocrine pancreatic insufficiency (EPI) measures which of the following?
A. Fecal canine pancreatic elastase
B. Fecal canine proteolytic activity
C. Serum canine pancreatic lipase immunoreactivity
D. Serum canine trypsin-like immunoreactivity

**CORRECT ANSWER: D**

Canine trypsin-like immunoreactivity is the most sensitive and specific commercially available diagnostic test for evaluation of EPI in dogs.⁴ Although dogs with EPI may have serum pancreatic lipase immunoreactivity concentrations below the lower limit of the reference range, there is overlap between healthy dogs and dogs with EPI, making serum pancreatic lipase immunoreactivity the inferior test as compared with the canine trypsin-like immunoreactivity assay.² Fecal proteolytic activity is generally decreased in dogs with EPI, but it can also be decreased in dogs with intestinal diseases; thus, a fecal proteolytic activity test lacks the specificity required to diagnose EPI.³ Like fecal proteolytic activity, fecal elastase can be a good screening test for EPI, but, because fecal elastase can also be decreased with other conditions, this test also lacks specificity.⁴
QUESTION 2
The owner of the dog in question 1 read online about potential causes of the dog’s GI signs and started the dog on fresh raw bovine pancreas approximately 5 days prior to presentation.

Before the dog is evaluated for EPI, which of the following should be recommended?
A. Fasting the dog to improve accuracy of the canine trypsin-like immunoreactivity test
B. Feeding the dog to improve accuracy of the canine trypsin-like immunoreactivity test
C. Stopping the raw bovine pancreas, as it is not effective, and testing for EPI
D. Stopping the raw bovine pancreas 7 days before testing for EPI

Correct Answer: A

Lipemia has the potential to affect canine and feline trypsin-like immunoreactivity assays; severe lipemia can result in spuriously high or low results. Canine and feline trypsin-like immunoreactivity tests are species-specific and will not cross-react with bovine or other pancreatic enzymes present in food. Raw pancreas can be used as an enzyme replacement in dogs with EPI but must be uncooked and fed immediately when fresh or kept frozen prior to use. Although there have been no reports of transmission of bacterial enteropathogens to dogs that have received raw pancreas, the owner should be made aware of the potential risk.

Canine and feline trypsin-like immunoreactivity tests are species-specific and will not cross-react with bovine or other pancreatic enzymes present in food.

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Bruce, an 11-year-old neutered male Labrador retriever, was presented for a hoarse bark and dysphonia, a 1-year history of increased respiratory noise, and a 4- to 6-month history of frequent and loud throat-clearing. The owners reported that he had also been increasingly intolerant of exercise for the past 6 months and occasionally stumbled on his pelvic limbs, which they attributed to arthritis and advanced age.

**Presentation**

On presentation, Bruce was panting and appeared anxious and excited. Marked upper respiratory stridor and associated cyanosis were noted, and SpO₂ was 87%. Acepromazine (0.03 mg/kg IV) was administered with flow-by oxygen. Within 5 minutes, Bruce’s respiratory effort had decreased and his mucous membranes were pink, with a capillary refill time <2 seconds; SpO₂ was 98%.

**Physical Examination**

Physical examination under acepromazine sedation revealed a temperature of 102.8°F (39.3°C), pulse of 96 bpm, and respiratory rate of 20 breaths/minute.

Weight was 77 lb (35 kg), and BCS was 6/9. When roused, Bruce had notable inspiratory stridor localized...
on auscultation to the laryngeal region. Cardiopulmonary auscultation revealed referred upper airway sounds. The abdomen was soft and compliant to palpation, and no lymphadenopathy was noted. A neurologic examination was not performed because of sedation.

**Diagnosis**

Three-view thoracic radiographs disclosed a mild diffuse bronchial pattern, most likely age related, and a small amount of air in the cervical esophagus consistent with aerophagia. No signs of pneumonia or megaeosophagus were noted. Cardiac silhouette and pulmonary vasculature were unremarkable. A lateral cervical radiograph demonstrated no abnormalities. Results of CBC, serum chemistry profile, and urinalysis were within reference ranges.

An upper airway examination was performed after administration of propofol (initially 4 mg/kg IV then titrated to the patient’s response) followed by doxapram (1 mg/kg IV bolus) to enhance respiratory excursions. Bilateral, flaccid, and complete laryngeal paralysis was noted, with decreased laryngeal sensitivity and erythematous corniculate processes. No abnormalities were noted on palpation of the larynx and trachea.

**DIAGNOSIS:**

**PRESUMPTIVE GERIATRIC ONSET LARYNGEAL PARALYSIS POLYNEUROPATHY**

Bruce was diagnosed with presumptive geriatric onset laryngeal paralysis polyneuropathy (GOLPP) based on his typical signalment (ie, elderly Labrador retriever) and the absence of other causes of laryngeal paralysis (eg, thyroid or mediastinal tumor, trauma). Historically, the onset of laryngeal paralysis in older dogs was called *idiopathic laryngeal paralysis* and was characterized as a bilateral mononeuropathy of the recurrent laryngeal nerves due to unknown etiology. More recent studies have concluded that the condition is very often a slowly progressive polyneuropathy, with laryngeal and esophageal dysfunction as the earliest manifestation. Although conditions such as myasthenia gravis and hypothyroidism have been associated with laryngeal paralysis, the associations are rare or unsubstantiated. In GOLPP, all of the intrinsic laryngeal muscles are affected, resulting in a flaccid laryngeal paralysis. Dogs can neither adduct nor abduct their arytenoids. GOLPP affects elderly dogs (ie, 8-13 years of age), most commonly Labrador retrievers. Other breeds, including Newfoundlands, greyhounds, Australian shepherd dogs, golden retrievers, Brittany spaniels, and some crossbreed dogs, also can be affected. Bruce’s owners were advised that, although cricoarytenoid laryngoplasty (ie, “tie-back”) surgery significantly improves quality of life and survival, he was likely to develop a slowly progressive, nonpainful, generalized neuropathy over the next several years.

In dogs with GOLPP, evaluation of esophageal function is recommended, as the severity of dysfunction is correlated with developing aspiration pneumonia following cricoarytenoid laryngoplasty. If an esophagram is not performed, an estimate of dysfunction can be based on clinical signs of regurgitation, coughing, and/or throat-clearing; however, this underestimates dysfunction. Because Bruce required sedation on presentation, an esophagram could not be performed and was declined at a follow-up appointment. Neurologic examination was also precluded at presentation because of sedation. Approximately one-third of dogs display early signs of generalized neuropathy at the time of diagnosis.

**Treatment & Long-Term Management**

Because of his critical respiratory condition and following discussion with his owners, Bruce immediately underwent a left-sided cricoarytenoid laryngoplasty under general anesthesia to permanently affix the left glottis in an abducted position. He received metoclopramide (1-2 mg/kg CRI every 24 hours) during surgery and omeprazole (1 mg/kg PO) 24 hours before surgery and 1 hour before surgery. Of note, recent studies show that
Thoracic and neck imaging should be performed in patients with airway compromise. A thorough upper airway examination using doxapram to stimulate robust respiratory efforts should be completed. Cricoarytenoid laryngoplasty should be performed to alleviate signs of upper respiratory obstruction. Pure µ agonists should be avoided perioperatively. The esophagus should be suctioned prior to extubation. Cisapride can be prescribed, as it may decrease the incidence of aspiration pneumonia.

Esophageal suctioning was performed shortly after induction and intubation, before leaving the operating room, and immediately prior to extubation. Adequate abduction of the left arytenoid was confirmed postoperatively by direct visualization on extubation (Figure).

Bruce recovered uneventfully from general anesthesia. The following morning, his rectal temperature was 100.5°F (38°C), and thoracic auscultation disclosed no abnormalities. He was hand-fed large meatballs, ate well, and was discharged later that day. His healthy appetite was a positive sign of recovery, as the earliest signs of aspiration pneumonia are pyrexia, inappetence, and lethargy. At-home medications included codeine (2 mg/kg PO every

### TREATMENT AT A GLANCE

- Thoracic and neck imaging should be performed in patients with airway compromise.
- A thorough upper airway examination using doxapram to stimulate robust respiratory efforts should be completed.
- Cricoarytenoid laryngoplasty should be performed to alleviate signs of upper respiratory obstruction.
- Pure µ agonists should be avoided perioperatively.
- The esophagus should be suctioned prior to extubation.
- Cisapride can be prescribed, as it may decrease the incidence of aspiration pneumonia.

GOLPP = geriatric onset laryngeal paralysis polyneuropathy

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**FIGURE** Per os view of the laryngeal aditus. Appearance of the paralyzed larynx before surgery (A). Neither adduction on sensitivity testing nor abduction on administration of doxapram was noted. Immediate postoperative appearance of the rima glottidis following left-sided cricoarytenoid laryngoplasty (B). This procedure provides a permanent, asymmetric widening of the paralyzed glottis, immediately relieving signs of respiratory obstruction.
6 hours for 3 days), trazodone (≈3 mg/kg PO every 12 hours for 7 days), and cisapride (0.5 mg/kg PO 30 minutes before breakfast and dinner and just before bedtime, for life). Cisapride is a prokinetic agent that may be prescribed as a long-term therapy to reduce gastroesophageal reflux and the risk for aspiration pneumonia. Bruce was assumed to have some degree of esophageal dysfunction because of his history of throat-clearing and because most dogs with GOLPP have esophageal dysfunction. Cisapride can be increased up to 1 mg/kg per oral dose if no diarrhea or abdominal discomfort is noted.

Bruce’s owners were advised to prevent him from drinking too much water at one time, as this can lead to regurgitation and increased risk for aspiration pneumonia. His activity level was limited for 10 to 14 days. A physical therapy program was strongly recommended. Wading in water and swimming with his head above the water (but no diving for balls) was also encouraged. A harness rather than a collar is preferred for leash attachment to avoid sudden pressure or shear force around the laryngeal region.

At the 1-month postoperative recheck appointment, neurologic examination, including assessment of gait, muscle tone, muscle atrophy, postural reactions, patellar reflexes, and flexor withdrawal reflexes in the pelvic and thoracic limbs, showed mild ataxia without significant weakness. Bruce had mild conscious proprioceptive deficits in both pelvic limbs, and mild muscle atrophy was noted around the semimembranosus and semitendinosus musculature.

Prognosis & Outcome
A successful cricoarytenoid laryngoplasty will immediately alleviate signs of upper respiratory obstruction and significantly improve quality of life. Because knowledge of laryngeal anatomy and experience with cricoarytenoid laryngoplasty technique are essential, this procedure should be performed by a board-certified surgeon. Some throat-clearing may persist for several months or may be permanent.

The most common postoperative complication is aspiration pneumonia, which occurs in ≈18% of cases without cisapride treatment. Most cases of aspiration pneumonia respond well to medical management with antibiotics, thoracic coupling, and, if indicated, oxygen supplementation. When patients are discharged following surgery, owners must be educated to watch for the earliest signs of aspiration pneumonia (ie, inappetence, lethargy, fever) followed by soft coughing.

In patients with GOLPP, neurodegeneration typically progresses insidiously over several years, with dogs developing muscle atrophy around the pelvic limbs, torso, and temporal musculature and becoming weaker with decreased proprioceptive responses. Strength (eg, water treadmill, sit-to-stand), balancing, and coordination exercises are recommended as long-term therapy for all affected dogs, with a goal of maintaining muscle mass and increasing awareness of limb placement. Daily walks are also recommended. Dogs may show no signs of pain and can survive for several years postoperatively with an excellent quality of life. Helping harnesses may be used by owners when their dogs begin to have difficulty standing and walking. Some owners may use a cart. Owners typically request euthanasia when their dog becomes nonambulatory or has repeated episodes of aspiration pneumonia.
At the author’s clinic, the average age of dogs presented with GOLPP is 11.3 years, with an expected survival time of 2 to 4 years following surgical intervention. Many dogs die from conditions unrelated to GOLPP. A 2016 study demonstrated a 7-year postoperative survival rate of 75% in affected dogs. Dogs with GOLPP should be evaluated for neurodegenerative signs every 6 months. Regular communication between owners and veterinarians, including owner education on GOLPP management, is key to a successful long-term outcome.

Bruce responded well to treatment. Two-and-a-half years after undergoing left-sided cricoarytenoid laryngoplasty, his respiratory rate and effort were normal at rest, with mild stridor on exertion from untreated right-sided flaccid laryngeal paralysis. He was continuing to receive cisapride and had not had any episodes of aspiration pneumonia. He underwent regular physical therapy twice weekly (see Video) and enjoyed wading in a lake. Bruce had mild to moderate muscle wasting of the pelvic limbs, needed assistance getting into the car, and had difficulty ascending stairs; his owners used a harness to help him with these activities.

**References**


**Suggested Reading**


**TAKE-HOME MESSAGES**

- GOLPP is a common condition in older dogs and is characterized by laryngeal paralysis, esophageal dysfunction, and a slowly progressing, nonpainful, generalized neuropathy.
- GOLPP can cause severe upper respiratory compromise.
- Outcomes from cricoarytenoid laryngoplasty (“tie-back”) are generally excellent when performed by experienced surgeons.
- Early recognition of aspiration pneumonia in patients with GOLPP allows early intervention and can improve patient outcome.
- Medical management of swallowing dysfunction may prevent aspiration pneumonia.
- Physical therapy exercise programs can help maintain ambulation.
- Owner education and long-term follow-up can ensure a successful outcome.®

GOLPP = geriatric onset laryngeal paralysis polyneuropathy

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**Video**

Bruce enjoyed wading in a lake. Video: https://www.youtube.com/watch?v=1234567890
A 6-month-old spayed American pit bull terrier crossbreed is presented for evaluation of severe pruritus and multifocal areas of alopecia and erythema. When the owners rescued the dog 2 months prior, the dog was pruritic around the eyes and licked its paws. The skin has since become progressively worse and the dog has gotten progressively more pruritic. The owners have been feeding a strict limited-ingredient diet without improvement.

Physical examination reveals crusts on the lateral cervical region and diffuse erythroderma. All distal limbs and both dorsal and ventral aspects of all paws are severely erythematous and crusted. The ventral abdomen and inguinal region have multifocal papules and pustules. An impression smear reveals intracellular and extracellular cocci bacteria (too numerous to count) with streaming neutrophils. Deep skin scrapings from the right forepaw and dorsal muzzle reveal 15 live adult *Demodex canis* mites, 2 juvenile *Demodex canis* mites, and 5 *Demodex canis* eggs per slide.
Which of the following drugs would be appropriate for this patient?

Based on the information provided, how would you grade the following drugs and why?

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<thead>
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<th>Drug</th>
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TURN THE PAGE TO COMPARE YOUR RESULTS
Did you answer?

The following represents the best responses based on drug metabolism, pharmacokinetics, species, diagnostic differentials, clinical and laboratory data, and other pertinent findings.

**Prednisone**

Although glucocorticoids are frequently used to help relieve pruritus, juvenile-onset generalized demodicosis is caused by underlying immune dysregulation, and glucocorticoid use could further suppress the immune system and exacerbate the demodicosis. Thus, prednisone is contraindicated in the treatment of demodicosis. In addition, this patient’s pruritus is likely caused by secondary bacterial infection, which prednisone would have no effect on.

**Oclacitinib**

Oclacitinib is frequently used to relieve pruritus. However, it is labeled for the control of pruritus associated with allergic dermatitis and control of atopic dermatitis, not for pruritus associated with demodicosis and bacterial infection, as in this patient. It is also labeled for dogs at least 12 months of age. Oclacitinib may actually increase the patient’s susceptibility to infection and demodicosis\(^1\) and may exacerbate demodicosis; its use is contraindicated in the treatment of demodicosis. A higher demodicosis incidence was noted when juvenile dogs were treated with elevated oclacitinib doses for extended time periods.\(^1\)

**Lokivetmab**

Lokivetmab is a monoclonal antibody that acts against interleukin-31, the “itch cytokine.” It is labeled for treatment of chronic itch due to allergic or atopic dermatitis. Lokivetmab may be effective at reducing this patient’s pruritus, but this use would be extra-label. Adverse effects are minimal, so use could be considered in this case to help improve the patient’s quality of life.

**Ivermectin**

Until recently, high-dose ivermectin, when well-tolerated, was the treatment of choice for demodicosis in dogs. Although it is effective, some dogs are sensitive to the drug and may experience side effects such as ataxia, mydriasis, tremors, stupor, hypersalivation, and respiratory arrest. These adverse effects are most commonly seen in dogs that are homozygous for a genetic defect in the multidrug sensitivity gene (\(MDR1\) gene, also known as \(ABCB1-1\) gene) that encodes for a p-glycoprotein pump that is an essential part of the blood–brain barrier. Dogs can be tested for the \(MDR1\) mutation via submission of a cheek saliva swab. However, some dogs with normal \(MDR1\) genotype still experience ivermectin sensitivity, so alternative mechanisms for increased sensitivity are likely.\(^2\) Although ivermectin can be used in this patient, there are safer treatment options with similar efficacy. Care should be used with ivermectin when the patient’s \(MDR1\) status is unknown.
Sarolaner

Although extra-label and not approved for treatment of demodicosis, new acaricides belonging to the isoxazoline class of parasiticides are the treatment of choice for generalized demodicosis.3-7 Isoxazoline acaricides function by selective inhibition of arthropod γ-aminobutyric acid– and L-glutamate–gated chloride channels. They have been shown to be effective for the treatment of generalized demodicosis in dogs.3-7 Administration of each medication should follow the normal recommendations for flea and tick control for each individual medication. Adverse effects of isoxazolines are rare, but can include vomiting and diarrhea. Isoxazolines have also been associated with neurologic adverse reactions, including tremors and seizures in rare cases.8

Amitraz Dip

Amitraz is the only licensed product in the United States for the treatment of generalized demodicosis. Its use has been associated with numerous adverse events, including sedative effects, allergic skin reactions, increased pruritus, hypothermia, hypotension, bradycardia, and hyperglycemia. Exposure to amitraz can also cause side effects (eg, migraine-like headaches, asthma attacks) in humans administering the medication. Because of these effects, the time-intensive administration, and availability of more effective alternatives, amitraz is not frequently used, and the commercial manufacturer discontinued sale of the drug in the United States in 2018. Although amitraz can be used in this patient, there are safer, more effective therapies for the treatment of generalized demodicosis.

Enrofloxacin

Although the impression smear was consistent with a bacterial infection (ie, secondary pyoderma), enrofloxacin—and all other fluoroquinolones—should not be used in this patient. Fluoroquinolones are considered second-tier antimicrobials that should only be used when topical therapy and first-tier systemic antimicrobials are not appropriate and supported by cultures and susceptibility panels. Fluoroquinolones have been associated with the development of methicillin resistance in Staphylococcus spp bacteria.9 In addition, fluoroquinolones should be used with caution in young, growing puppies due to the potential for cartilage deformities and joint growth disorders.

Cephalexin

Cephalexin (a first-generation cephalosporin) or clindamycin can be considered to treat this patient’s secondary bacterial pyoderma. These are considered first-tier antimicrobials and are a good choice for empiric therapy.3 Treatment is recommended at the higher end of the dose range and should be continued for at least 1 week beyond clinical resolution.
**Benzoyl Peroxide Shampoo**

Frequent bathing with a benzoyl peroxide-containing shampoo is often helpful in the treatment of generalized demodicosis and secondary infections. Benzoyl peroxide shampoos have been considered the best choice for adjunctive treatment of demodicosis due to their antibacterial and follicular flushing properties. If a benzoyl peroxide shampoo is too drying on a weekly bathing interval, a chlorhexidine-based product can be used. Chlorhexidine-based shampoos at 3% to 4% concentration or 2% concentration when combined with 2% miconazole have been shown to be more effective at treating bacterial or *Malassezia* spp skin infections and are typically not as drying as benzoyl peroxide-based shampoos. Chlorhexidine-based shampoos are typically the product of choice for skin infections but lack the follicular flushing properties of benzoyl peroxide shampoos.

**Gentamicin/Betamethasone Spray**

Because of the potent corticosteroid (ie, betamethasone) in these combination products, localized immunosuppression can occur where the product is sprayed and cause exacerbation of the demodicosis. Therefore, its use is not recommended.

**Conclusion**

Regardless of the treatment choice for this patient’s generalized demodicosis, miticidal treatment should continue until multiple consecutive skin scrapes obtained a month apart are completely negative for all evidence of *Demodex* spp mites. Antibiotic therapy should continue until at least 1 week beyond clinical resolution of all superficial bacterial skin infection. Because there is a genetic component causing a predisposition to the development of juvenile generalized demodicosis, affected dogs should not be bred.

**References**


**Suggested Reading**

ALI NEMETH, DVM, is completing a small animal rotating internship at Tufts Veterinary Emergency Treatment & Specialties in Walpole, Massachusetts. She earned her DVM from Cummings School of Veterinary Medicine at Tufts University.

CASE IN POINT PAGE 17

ANDREW ROSENBERG, DVM, DACVD, is the practice owner of Animal Dermatology & Allergy Specialists and practices in both the Riverdale, New Jersey, and Westchester County, New York, locations. He earned his Bachelor of Science with distinction in research and his DVM from Cornell University and completed his residency with Animal Dermatology Clinic in Tustin, California. Dr. Rosenberg received the ACVD Resident Research Award for his work in cyclosporine-associated gingival overgrowth and currently serves as the Chair for the ACVD Education Committee. His clinical interests include allergies and autoimmune skin diseases. Dr. Rosenberg also treats skin conditions of animals in zoos and wildlife centers on a volunteer basis.

RED LIGHT, GREEN LIGHT PAGE 62

THOMAS SCHERMERHORN, VMD, DACVIM (SAIM), is a professor of small animal medicine and the Morgan K “Al” Jarvis Chair of Veterinary Medicine at Kansas State University, where his laboratory focuses on cellular and molecular endocrinology, particularly the study of diabetes mellitus and related metabolic disorders in dogs and cats. Dr. Schermerhorn completed a medical internship at South Shore Veterinary Associates in South Weymouth, Massachusetts, and a residency in small animal internal medicine at Cornell University, where he also received research training as a graduate fellow in the department of molecular medicine. His clinical interests include canine and feline endocrinology, particularly diabetes mellitus.

CONSULT THE EXPERT PAGE 27

BRYDEN J. STANLEY, BVMS, MANZCVS, MRCVS, MVetSc, DACVS, is an associate professor at Michigan State University. She earned her veterinary degree from Murdoch University in Australia before completing a surgery residency and earning her master’s degree from University of Saskatchewan in Canada. Dr. Stanley’s clinical interests include aspects of soft tissue surgery; her research interests are upper respiratory conditions and wound healing. She publishes frequently, has received many teaching awards, and lectures widely nationally and internationally.

CASE IN POINT PAGE 57
I have been using lasers in my equine-only practice. The CO₂ laser’s wavelength of 10.6 μm is well absorbed by soft tissue, this unique aspect of the CO₂ laser enables precise dissection and vaporization of soft tissue with minimum hemorrhage as well as reduced postoperative pain and swelling (due to the coagulation of nerve endings and lymphatics along the edges of incisions). Whether doing incisions, excisions, dissections or ablations, CO₂ laser surgery is always noncontact; therefore it minimizes tissue trauma while providing a strong sterilizing effect by killing surface bacteria.

**CO₂ Laser Uses**

With my CO₂ laser, I have been impressed with the reduced inflammation and swelling of the surgery sites, especially in cases involving castration of the mature stallion. Small bleeders may be controlled by raising the handpiece away from the tissue, defocusing the laser beam, and coagulating the affected surface of the vessel wall.

After performing closed castration in normal stallions (see Figures 1 and 2), we see horses returning to training very quickly and without the threat of evisceration. Further, my laser’s flexible waveguide enables superior reach and ergonomics during operation in this area (more on this later).

I also use the CO₂ laser a lot for tumor debulking and ablation. Having used cryotherapy for tumor therapy for over 30 years, I now perform almost all treatments with the CO₂ laser. Tumors I regularly deal with include melanomas, squamous cell carcinomas, mastocytomas, and equine sarcoids.

The 40-watt Aesculight CO₂ laser has impressive ability to treat large tumor masses. It is useful for treating cutaneous tumors in the horse, including equine sarcoma, squamous cell carcinoma, and melanoma. Tumor debulking, ablation, and dissection with limited hemorrhage are facilitated with the CO₂ laser. It enables thermal coagulation of the surgical margins; the thermal effect assists in eliminating abnormal cells left by conventional surgical techniques. The laser thermally seals blood and lymphatic vessels by which the microscopic tumors spread; this, with decreased tissue manipulation, decreases the rate of tumor seeding and recurrence.

The use of the laser in treating melanomas in the gray horse is illustrated in Figure 3 (pre-operative), Figure 4 (intra-operative), and Figure 5 (immediately post-operative).

**CO₂ Laser Power Settings**

The power of the CO₂ laser is critically important for high quality incisions, excisions and dissections performed in one path with minimum thermal damage to the margins—the higher the power, the faster the incision can be performed without multiple back and forth movements of the laser beam. Equally important is the power of the laser for large area ablations—the higher the power, the larger the area that can be treated in the minimum amount of time. Thus, higher laser power is preferred, especially for equine and large animal surgical procedures.

Last year I upgraded to a 40 watt Aesculight CO₂ laser. It is the highest power CO₂ laser for veterinary use, and it is the only flexible waveguide fiber laser on the market with extended reach appropriate for open field equine surgery, as illustrated in Figure 1.

**Beam Delivery and Accessories**

The flexible waveguide fiber allows easier handling of the laser handpiece with a greater control of beam spot size and the benefit of rapid defocusing for safety and versatility. My laser handpieces also have a relatively shorter tip-to-tissue distance, are more precise and offer multiple-spot sizes while articulated arm lasers do not. The flexible fiber is ergonomic and easy to use, unlike the heavier articulated arm laser that I previously owned.

There are several important laser accessories that I use regularly. In addition to a regular laser handpiece with interchangeable laser tips of different lengths and focal spot sizes (Figure 4), the adjustable tipless handpiece (Figures 1-2) allows for more options like changing the laser spot size intraoperatively without changing the handpiece.

The handpiece incorporates four spot sizes: 0.25 mm and 0.4 mm spot sizes for excisions, incisions and dissections, and 0.8 mm and 1.4 mm for large-area surface ablations. The other tipless handpiece design with fixed, interchangeable spot size nozzles enables more visibility and improves handling ergonomics. Also, Aesculight’s exclusive “paintbrush” laser tip produces a 3 mm x 0.4 mm beam useful for ablating of large surface areas at the highest laser power settings.

**Summary**

The main advantages of the CO₂ wavelength technology for soft tissue surgery include reduced tissue trauma, precise dissection, sterilization of the tissue surface (as the laser beam kills surface bacteria), reduced operative hemorrhage, quickened healing and reduced post-operative pain. My clients regularly comment on how good the surgical sites look.
REFERENCES:


WATCH CO₂ LASER SURGERY VIDEOS:
www.Aesculight.com/video/

About Dr. Fleck:
Dr. Fleck is a graduate of the University of California, Davis. He founded the Rainland Farm Equine Clinic in 1975 and has expertise in nuclear scintigraphy (bone scan), lameness examinations and breeding as well as reconstructive, laser and arthroscopic surgery.
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-Naphthalene-carboxamide, 4-[(3-chloro-5-(trifluoromethyl)-phenyl)-(4, 5-dihydro-5-(trifluoromethyl)-1-isoxazolyl)-N-[2-oxo-2-[2,2-trifluoromethyl]laminoo]ethyl].

Indications:
NexGard kills adult fleas and is indicated for the treatment and prevention of flea infestations (Cheesyheadsis 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 fleas.

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:

<table>
<thead>
<tr>
<th>Body Weight</th>
<th>Afoxolaner Per Chewable (mg)</th>
<th>Chewables Administered</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.0 to 10.0 lbs</td>
<td>11.3</td>
<td>One</td>
</tr>
<tr>
<td>11.1 to 24.0 lbs</td>
<td>28.3</td>
<td>One</td>
</tr>
<tr>
<td>24.1 to 66.0 lbs</td>
<td>88</td>
<td>One</td>
</tr>
<tr>
<td>66.1 to 121.0 lbs</td>
<td>136</td>
<td>One</td>
</tr>
<tr>
<td>Over 121.0 lbs</td>
<td>Administer the appropriate combination of chewables</td>
<td></td>
</tr>
</tbody>
</table>

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 other drugs out of the reach of children. In case of accidental ingestion, consult 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.

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Afoxolaner</th>
<th>Oral active control</th>
</tr>
</thead>
<tbody>
<tr>
<td>N1</td>
<td>% (n=415)</td>
<td>N2</td>
</tr>
<tr>
<td>Vomiting (with and without blood)</td>
<td>17</td>
<td>4.1</td>
</tr>
<tr>
<td>Dry/Foamy Skin</td>
<td>13</td>
<td>3.1</td>
</tr>
<tr>
<td>Diarrhea (with and without blood)</td>
<td>13</td>
<td>3.1</td>
</tr>
<tr>
<td>Lethargy</td>
<td>7</td>
<td>1.7</td>
</tr>
<tr>
<td>Anorexia</td>
<td>5</td>
<td>1.2</td>
</tr>
</tbody>
</table>

1Number of dogs in the afoxolaner treatment group with the identified abnormality.
2Number 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/animal/veterinary/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 >90% effectiveness at eight hours. In a separate well-controlled laboratory study, NexGard demonstrated 100% effectiveness against adult fleas 24 hours post-infection 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-infection. Dogs in both the treated and control groups that were infected 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-infection, fleas from dogs in the treated group were essentially unable to produce any eggs (0-1 eggs) while fleas from 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 88.0%, 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 >87% effectiveness against Dermacentor variabilis, >94% effectiveness against Ixodes scapularis, and >50% effectiveness against Rhipicephalus sanguineus, 48 hours post-infection for 30 days. At 72 hours post-infection, 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 infected 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 (8.3 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 chemistry, 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 tx 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 anti-histamines. 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® (afoxolaner) Chewables is available in four sizes of beef-flavored soft chewables: 11.3, 28.3, 68, and 136 mg afoxolaner. Each chewable size is available in color-coded packages of 1, 3 or 6 chewables. 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/animal/veterinary/SafetyHealth.
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1. **CONSULT THE EXPERT** PAGE 11
   Antimicrobial resistance, or the risk that it may occur, should be suspected if a patient has received multiple broad-spectrum antimicrobial courses or antimicrobial treatment within the past _______ months.
   A. 3
   B. 6
   C. 9
   D. 12

2. **CASE IN POINT** PAGE 17
   Which of the following might be included in a differential diagnoses list for a patient with generalized bone marrow hypoplasia/aplasia?
   A. Infectious disease
   B. Myelophthisic disease
   C. Immune-mediated disease
   D. All of the above

3. **CONSULT THE EXPERT** PAGE 27
   Which of the following is not an advantage of assessment of clinical signs as a monitoring method for diabetic cats and dogs?
   A. It involves the owner in the pet’s care.
   B. A significant disturbance in blood glucose can be inferred from the persistence or emergence of clinical signs during treatment.
   C. Chronic, mild to moderate blood glucose disturbances are readily detected.
   D. Absence of clinical signs is associated with improved quality of life.

4. **CASE IN POINT** PAGE 57
   Which of the following statements regarding geriatric onset laryngeal paralysis polyneuropathy (GOLPP) is false?
   A. GOLPP is slowly progressive.
   B. GOLPP typically occurs secondary to myasthenia gravis.
   C. Use of cisapride in patients with GOLPP may decrease incidence of aspiration pneumonia.
   D. Use of perioperative pure µ agonists should be avoided in patients with GOLPP.

5. **RED LIGHT, GREEN LIGHT** PAGE 62
   _____________ would be an appropriate treatment option for a dog with generalized demodicosis.
   A. Prednisone
   B. Oclacitinib
   C. Sarolaner
   D. Gentamicin/betamethasone spray

**Answer Key:**
1: A  2: D  3: C  4: B  5: C
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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.NexGardClinic.com.

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See page 70 for product information summary.