BREED-SPECIFIC CONSIDERATIONS TO AVOID ADVERSE DRUG EFFECTS

IN THIS ISSUE

- Enteral & Parenteral Nutrition in the Intensive Care Unit
- Pelvic Limb Amputation Step by Step
- Case Report: Electrocution Emergency in a Puppy
- Differential Diagnoses for Hypernatremia
Guarantee compliance and make ear infections easier

Treat your patients’ most common otitis externa infections with one dose administered by you.

Claro® is indicated for the treatment of otitis externa in dogs associated with susceptible strains of yeast (Malassezia pachydermatis) and bacteria (Staphylococcus pseudintermedius).

CAUTION: Federal (U.S.A.) law restricts this drug to use by or on the order of a licensed veterinarian. PRECAUTIONS: For use in dogs only. Do not use in cats (see POST APPROVAL EXPERIENCE). CLARO® has been associated with rupture of the tympanic membrane. Reevaluate the dog if hearing loss or signs of vestibular dysfunction are observed during treatment. Signs of internal ear disease such as head tilt, vestibular signs, ataxia, nystagmus, facial paralysis, and keratoconjunctivitis sicca have been reported (see POST APPROVAL EXPERIENCE) with the use of CLARO®. Wear eye protection when administering CLARO®. (see Human Warnings, PRECAUTIONS, POST APPROVAL EXPERIENCE).

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See page 2 for product information summary.
TODD ARCHER, DVM, MS, DACVIM (SAIM), is an associate professor of small animal internal medicine at Mississippi State University, where he also earned his DVM and MS and completed an internship and residency in small animal internal medicine. Dr. Archer’s clinical interests include endocrinology, hematology, immunology, and interventional radiology.

DIFFERENTIAL DIAGNOSIS PAGE 20

DANIEL L. CHAN, DVM, DACVECC, DECVECC, DACVN, FHEA, MRCSV, is professor of emergency and critical care medicine and clinical nutrition and head of the department for clinical science and services at The Royal Veterinary College, University of London. He earned his DVM from Cornell University, completed a small animal internship at Animal Medical Center in New York City, New York, and completed a dual residency in emergency and critical care medicine and clinical nutrition at Cummings School of Veterinary Medicine at Tufts University. Dr. Chan is also the Editor-in-Chief of Journal of Veterinary Emergency and Critical Care.

MICHAEL H. COURT, BVSc, PhD, DACVAA, holds the William R. Jones Endowed Professorship at Washington State University. He received his veterinary training from University of Queensland in Brisbane, Australia, his anesthesia specialty training from Cummings School of Veterinary Medicine at Tufts University, and his pharmacogenomics research training from Tufts University School of Medicine. Dr. Court has authored numerous articles on pharmacology research. He received a Special Emphasis Research Career Award from the National Institutes of Health, the Frank K. Ramsay Invited Lectureship, and the Pfizer Award for Research Excellence. His current research goal is to develop genetic tests that enable identification of dogs susceptible to development of severe adverse effects from drugs used for anesthesia, in surgery, and for treatment of pain.

TOP 5 PAGE 71

KRISTEN FRENCH-KIM, DVM, earned her DVM from The Ohio State University in May 2021. She has a research background in immunology, vaccine research, and anatomic pathology and is interested in pursuing a career in small animal surgery.

PROCEDURES PRO PAGE 23

JENNIFER GOOD, DVM, DACVECC, is a clinical assistant professor in the emergency and critical care department at University of Georgia. She earned her DVM from Cornell University and completed a small animal internship at Oradell Animal Hospital in Paramus, New Jersey, and a small animal emergency and critical care residency at University of Pennsylvania. Dr. Good became certified in veterinary acupuncture via a mixed-animal program at the Chi Institute in Reddick, Florida. She has since performed acupuncture on large, small, and exotic animals at University of Georgia.
FROM
CLINICIAN’S BRIEF
ON SOCIAL MEDIA

WE ASKED …

Do you ever administer enrofloxacin IV in cats?

“No, we administer diluted SC or IM in cats and dogs.”—Dawn M

“So sometimes we do if it is necessary, but we typically administer SC.”—Pasorn P

“It gives me heebie-jeebies, but yes, we do when we need to!”—Sarah H

“Yes, diluted and slowly.”—Marta R

“I try to avoid administering enrofloxacin by any route in a cat.”—Lauren S

“Yes, but usually for sepsis.”—Sarah B

How do you discourage no-show appointments?

“We make notes in files and hold grudges forever.”—Erica I

“We have a cancellation policy. It ruffles a few feathers, but there needs to be mutual respect with pet owners.”—Chung M

“Discourage them? We get excited for a short break!”—Kathy J

“Generally nothing—just bottle feelings inside until they become a boiling caldron of bitter resentment. Recidivists however get either a gentle admonition or a stern berating depending on my mood.”—Ipswich Animal Hospital

Do you use tape stirrups when bandaging limbs?

91% Yes
9% No

How often do you administer levothyroxine to a patient per day?

79% Twice daily
21% Once daily

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Rapidly activate your patient’s unique gut microbiome for ultimate digestive health with breakthrough ActivBiome+ Technology.

Hill’s strongest digestive portfolio ever

Ask about microbiome nutrition that’s A STEP AHEAD FOR THEIR BEST LIFE
TOP 5
Top 5 Breed-Specific Considerations to Avoid Adverse Drug Effects
Katrina L. Mealey, DVM, PhD, DACVIM, DACVCP
Michael H. Court, BVSc, PhD, DACVAA

CONSULT THE EXPERT
Enteral & Parenteral Nutrition in the Intensive Care Unit
Daniel L. Chan, DVM, DACVECC, DECVECC, DACVN, FHEA, MRCVS

DIFFERENTIAL DIAGNOSIS
Hypernatremia
Todd Archer, DVM, MS, DACVIM (SAIM)

PROCEDURES PRO
Canine Pelvic Limb Amputation
James Howard, DVM, MS, DACVS
Kristen French-Kim, DVM
Stephen C. Jones, MVB, MS, DACVS
Nina R. Kieves, DVM, DACVS, DACVSMR, CCRT

CASE IN POINT
Electrocution Emergency in a Puppy
Jennifer Good, DVM, DACVECC
Pass the torch to a partner you can trust.

When you partner with CareVet you don’t need to choose between a strong offer for the hospital you’ve built and a great environment for you and your team after transitioning. CareVet is a partner you can trust in not only elevating your vision for your hospital and your career, but securing the future of your team, as well. Our Whole Person Approach concentrates on supporting each Team Member’s personal and professional needs for health, support, fulfillment and advancement.

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✓ Living Wage for all Hospital Team Members

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ON THE WEB

THIS MONTH’S FEATURED CLINICAL CONTENT AVAILABLE ONLY ONLINE

WEB EXCLUSIVE
Quiz: Metastasis or No Metastasis: Radiography & Ultrasonography
Katherine Suter, DVM
David M. Schmidt, DVM, DACVR
brief.vet/metastasis_quiz

PODCAST
Insulin Selection in Diabetic Dogs & Cats with Dr. Schermerhorn
Thomas Schermerhorn, VMD, DACVIM (SAIM), explains why no single insulin product is best, how to make initial insulin selections, how to use tests (eg, A1c, fructosamine) and interstitial monitors to assess insulin response, and when to consider switching insulins.
brief.vet/insulin_selection
JAMES HOWARD, DVM, MS, DACVS, is an associate professor of soft tissue surgery at The Ohio State University, where he also earned his DVM and completed a surgical residency. He also completed a rotating medicine and surgery internship at University of Tennessee. His research interests include hepatobiliary and GI surgery and endocrinopathies. Dr. Howard’s ongoing research includes minimally invasive diagnostic procedures, pharmacokinetics and pharmacodynamics, and evaluative hepatobiliary sampling techniques.

PROCEDURES PRO PAGE 23

STEPHEN C. JONES, MVB, MS, DACVS, is an assistant professor of small animal orthopedics at The Ohio State University. He earned his veterinary degree at University College Dublin in Ireland. Dr. Jones completed both a rotating and specialty surgery internship at the Hollywood Animal Hospital in Hollywood, Florida, and a combined residency in small animal surgery and MS at University of Florida. He has written numerous scientific papers, book chapters, and abstracts and lectures worldwide. His special interests include minimally invasive fracture repair, medical and surgical treatment of joint disease, arthroscopy, and surgical management of angular limb deformities.

PROCEDURES PRO PAGE 23

NINA R. KIEVES, DVM, DACVS, DACVSMR, CCRT, is an assistant professor of small animal orthopedics at The Ohio State University. She earned her DVM at University of Minnesota. Dr. Kieves’ research interests are sports medicine and rehabilitation and surgical treatment with minimally invasive techniques.

PROCEDURES PRO PAGE 23

KATRINA L. MEaley, DVM, PhD, DACVIM, DACVCP, is the Regents Professor and Endowed Chair and Director of the Program in Individualized Medicine at Washington State University. She earned her degree in Pharmacy from University of New Mexico and her DVM from Colorado State University. Dr. Mealey completed a small animal internship at University of Minnesota. She also completed residencies in small animal internal medicine and veterinary clinical pharmacology and earned her PhD in pharmacology at Texas A&M University. Dr. Mealey has authored numerous articles and book chapters, as well as Pharmacotherapeutics for Veterinary Dispensing. She received the Washington State University Woman of the Year Award and the Pfizer Award for Research Excellence. Dr. Mealey was elected as a Fellow of the US National Academy of Inventors and to the Washington State Academy of Sciences.

TOP 5 PAGE 71

IMOXI™ Topical Solution for Dogs and for Cats (imidacloprid + moxidectin)

BRIEF SUMMARY: Before using IMOXI™ Topical Solution for Dogs (imidacloprid + moxidectin) or IMOXI™ Topical Solution for Cats (imidacloprid + moxidectin), please consult the product insert, a summary of which follows:

CAUTION: Federal (U.S.A.) Law restricts this drug to use by or on the order of a licensed veterinarian.

IMOXI™ Topical Solution for Dogs:

• DO NOT ADMINISTER THIS PRODUCT ORALLY

For the first 30 minutes after application ensure that dogs cannot lick the product from application sites themselves or other treated dogs, and separate treated dogs from one another and from other pets to reduce the risk of accidental ingestion.

Ingestion of product by dogs can cause serious adverse reactions including depression, salivation, dilated pupils, incoordination, panting, and generalized muscle tremors. In avermectin sensitive dogs,* the signs may be more severe and may include coma and death.

* Some dogs are more sensitive to avermectins due to a mutation in the MDR1 gene. Dogs with this mutation may develop signs of severe avermectin toxicity if exposed to this product. The most common breeds associated with this mutation include Collies and Collie crosses.

If ingestion of drug by dogs is suspected, take off the collar and other treated dogs, and separate treated dogs from one another and from other pets to reduce the risk of accidental ingestion.

Ingestion of product by dogs can cause serious adverse reactions including depression, salivation, dilated pupils, incoordination, panting, and generalized muscle tremors. In avermectin sensitive dogs,* the signs may be more severe and may include coma and death.

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If ingestion of drug by dogs is suspected, take off the collar and other treated dogs, and separate treated dogs from one another and from other pets to reduce the risk of accidental ingestion.
THE PROTECTION PETS NEED AGAINST
BROAD-SPECTRUM EXCUSES

“My dog’s flea drops protect against heartworms”

“No pet should be vulnerable to fleas, heartworms or intestinal parasites. NEW generic Imoxi™ Topical Solution (imidacloprid + moxidectin) is a prescription topical combination that’s proven effective for broad-spectrum prevention at a price that’s easy on pet owners.

- Protects against fleas, heartworms, and intestinal parasites for a full month when used as directed
- Quick, easy application with new Twist-N-Go™ cap technology
- Brought to you by Vetoquinol, the same company that brings you other quality generic medications such as Vetprofen® (carprofen)

CAUTION: Federal (U.S.A) law restricts this drug to use by or on the order of a licensed veterinarian. Dogs: WARNING: DO NOT ADMINISTER THIS PRODUCT ORALLY. For the first 30 minutes after application, ensure that dogs cannot lick the product from application sites on themselves or other treated animals. Children should not come in contact with the application sites for two (2) hours after application. (See Contraindications, Warnings, Human Warnings and Adverse Reactions for more information.) Cats: Do not use on sick, debilitated, or underweight cats. Avoid oral ingestion. For additional safety information see brief on page 8 or visit www.vetoquinolusa.com/imoxi-info.

IMoxi™ Topical Solution
(imidacloprid + moxidectin)

VISIT WWW.IMOXITOPICAL.COM TO LEARN MORE.
CONSULT THE EXPERT

ENTERAL & PARENTERAL NUTRITION IN THE INTENSIVE CARE UNIT

Daniel L. Chan, DVM, DACVECC, DECVECC, DACVN, FHEA, MRCVS
The Royal Veterinary College, University of London
London, England
Nutritional support is essential for critically ill patients in the intensive care unit and should be included as part of the standard of care, as there are potentially serious consequences of malnutrition. Effective nutritional management strategies can alleviate the risk for development of malnutrition and associated morbidities.1,2
Inadequate food intake, GI dysfunction, and metabolic changes can cause malnourishment in hospitalized patients not supported with nutritional interventions. Critically ill patients catabolize lean body mass during periods of food and nutrient deprivation, emphasizing the need for nutritional support; this is also the case in obese patients, as critically ill patients with inadequate food intake preserve fat stores but catabolize lean body tissue. Cats do not downregulate gluconeogenesis or proteolysis during low protein intake. Continued loss of lean body mass can result in negative effects on wound healing, immune function, and, ultimately, clinical outcomes. Conversely, adequate energy substrates, protein, essential fatty acids, and micronutrients support wound healing and tissue repair.

**Nutritional Assessment**

Nutritional support carries a risk for complications (eg, hyperglycemia, electrolyte shifts, aspiration pneumonia), but these can be minimized through careful patient selection, nutritional assessment, and sound nutritional planning. A nutritional assessment should be performed through systematic evaluation to identify patients that require immediate nutritional support. Patients with obvious signs of malnutrition, >10% body weight loss, ≥3 days poor food intake, and prolonged illness should be given urgent nutritional support. Cardiovascular status should be stable and electrolyte, fluid, and acid-base abnormalities should be corrected before nutritional support is provided.

**Calculating Energy Needs**

Resting energy requirement (RER) is the number of calories required to maintain homeostasis while the patient is at rest. RER is calculated as 70 × body weight in kg0.75. In patients that weigh 4.4 to 66 lb (2-30 kg), 30 × body weight in kg + 70 can be used to approximate energy needs. RER has historically been multiplied by an illness factor between 1.1 to 2 to account for increases in metabolism associated with different conditions and injuries. Recently, less emphasis has been placed on these subjective illness factors, and current recommendations include using RER as a starting point and adjusting based on the response to feeding.

Although definitive studies determining the precise nutritional requirements for critically ill patients have not been performed, some recommendations are available. It is generally accepted that hospitalized dogs should be supported with 4 to 6 g of protein/100 kcal (15%-25% of total energy requirements) and cats should be supported with ≥6 g of protein/100 kcal (25%-35% of total energy requirements). Patients with poor protein tolerance (eg, those with hepatic encephalopathy) should receive reduced amounts of protein (dogs, ≈3 g/100 kcal; cats, 4 g/100 kcal). Patients with hyperglycemia or hyperlipidemia may also require decreased amounts of carbohydrates and lipids, respectively, when provided with parenteral nutrition.

**Enteral Nutrition**

Enteral nutrition is usually preferable, as it helps maintain GI structure and function. Nasoesophageal/nasogastric, esophagostomy, and gastrostomy feeding tubes are commonly used in dogs and cats. Considerations for various feeding tubes should be reviewed (Table). Guidance on placement of feeding tubes is available (see Suggested Reading, page 14). Most complications with feeding tubes include tube occlusion and localized irritation at the tube exit site. More serious complications include
infection at the exit site or, rarely, complete tube dislodgment and peritonitis with a gastrotomy tube (proper stoma require 10 days to form). Risk for complications can be reduced by using the appropriate tube, through proper food selection and preparation, and with careful monitoring.8,9

Feedings are generally administered every 4 to 6 hours, and feeding tubes should be flushed with 5 to 10 mL (based on size of patient and tube) of water before and after each feeding to minimize obstruction of the tube. At discharge, the number of feedings should be reduced to 3 to 4 times per day to help facilitate pet owner compliance.

A volume of 5 to 10 mL/kg per individual feeding is generally well-tolerated but can vary by patient. Enteral diets are mostly composed of water (most canned foods are already >75% water); thus, the amounts of fluids administered parenterally (including water from pre- and postfeeding flushes) should be adjusted to avoid volume overload. Premature removal of tubes can be prevented by using special collars (eg, Elizabethan) and wrapping the tube securely. Care should be taken to avoid tightly wrapping the tube, as this could lead to patient discomfort and even compromise proper ventilation.

### Parenteral Nutrition

Indications for parenteral nutrition include persistent vomiting, severe malabsorptive disorders, and severe ileus. Safe administration of IV nutrition requires a dedicated catheter placed using an aseptic technique; this should only be provided by a 24/7 care facility where close monitoring can be provided.7 Long catheters composed of silicone, polyurethane, or tetrafluoroethylene are recommended for use with parenteral nutrition to reduce the risk for thrombophlebitis.7 Most parenteral nutrition solutions contain a carbohydrate (dextrose), protein (amino acids), and fat (lipids) source. The proportions of each component in the admixture are determined based on the required energy and protein needs of the patient. Detailed instructions for formulation of parenteral nutrition admixtures are available.7 Compounding parenteral nutrition admixtures requires special equipment and is commonly sourced from human hospitals. Alternatively, there are a few commercially available, ready-made, 3-in-1 solutions (Figure, next page) that provide 40% to 70% of a patient’s RER (depending on the size of the patient) when administered at 2 to 4 mL/kg/hour; these solutions contain ≈20 mmol/L of potassium and therefore cannot be administered at higher rates.7

### TABLE
**CONSIDERATION FOR DIFFERENT TYPES OF FEEDING TUBES**

<table>
<thead>
<tr>
<th>Feeding Tube</th>
<th>Typical Duration of Use</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasoesophageal</td>
<td>Short-term (&lt;5 days)</td>
<td>Inexpensive, easy to place, no anesthesia required</td>
<td>Requires complete liquid diet, prone to being dislodged</td>
</tr>
<tr>
<td>Esophagostomy</td>
<td>Extended (weeks to months)</td>
<td>Inexpensive, simple to place, can accommodate high-calorie semiliquid diets</td>
<td>Requires brief anesthesia, prone to becoming obstructed, incision can become inflamed or infected</td>
</tr>
<tr>
<td>Gastrostomy</td>
<td>Extended (weeks to months)</td>
<td>Can accommodate high-calorie semiliquid diets</td>
<td>Requires general anesthesia for placement, endoscopic placement requires special equipment, tube displacement can result in peritonitis</td>
</tr>
</tbody>
</table>

RER = resting energy requirement
The osmolarity of these solutions can vary, but solutions of <600 to 750 mOsmol/L can be suitable for peripheral administration.\(^7\)

**Monitoring & Reassessment**

Daily monitoring of body weight in patients supported with nutritional interventions is recommended. However, fluid shifts should be accounted for when changes in body weight are evaluated; thus, BCS assessment is also important. Using RER as the patient’s caloric requirement as a starting point, the number of calories provided may need to be increased (typically by 25% if well-tolerated) to meet the patient’s changing needs. In patients unable to tolerate prescribed amounts, reducing amounts of enteral feedings and supplementing feed with parenteral nutrition should be considered.

Possible complications of parenteral nutrition include thrombophlebitis and metabolic disturbances (eg, hyperglycemia, electrolyte shifts, hypertriglyceridemia). Avoiding serious complications associated with parenteral nutrition requires early identification of problems and prompt action. Frequent monitoring of vital signs, catheter exit sites, and routine serum chemistry profiles can help identify developing problems. Persistent hyperglycemia while the patient is receiving nutritional support may require adjustment to the nutritional plan (eg, decreasing dextrose content in parenteral nutrition) or administration of regular, short-acting insulin.

Continual reassessment can help determine when to transition the patient from assisted feeding to voluntary consumption of food. Nutritional support should only be discontinued when the patient can consume ≈75% of their RER without support. In patients receiving parenteral nutrition, the transition to enteral nutrition should occur over at least 12 to 24 hours, depending on tolerance of enteral nutrition.

\[\text{RER} = \text{resting energy requirement}\]
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The American Veterinary Dental College greatly appreciates iM3 for their support for the practical portion of the 2021 AVDC certifying examination and their dedication to the advancement of veterinary oral and dental health.
2 OUT OF 5 WORMS RECOMMEND SIMPARICA TRIO®
(sarolaner, moxidectin, and pyrantel chewable tablets)

That’s because their one little chew misses two big parasites, tapeworms and whipworms.

Plenty of room to spread out without a care in the world. Thanks Trio!
– A. Tapeworm

Perfect spot for me and all the little Whippersnappers.
– A. Whipworm

We met the nicest gaggle of Whipworms.
– A. Whipworm
Plenty of room to spread out without a care in the world.

Thanks Trio!

– A. Tapeworm

2 OUT OF 5 WORMS RECOMMEND SIMPARICA TRIO® (sarolaner, moxidectin, and pyrantel chewable tablets)

That’s because their one little chew misses two big parasites, tapeworms and whipworms.

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Which would you choose?

One monthly chewable designed for defense of parasites that skips tapeworms, and whipworms [3x more common in US dog parks than roundworms]¹

OR

Two products that provide 360-degree protection against gross parasites, including tapeworms (which could have zoonotic potential) and whipworms

Don’t leave gaps in coverage

Ask your Elanco sales representative about 360-degree parasite protection or visit 360-degreeprotection.com.

Interceptor Plus Indications
Interceptor Plus is indicated for the prevention of heartworm disease caused by Dirofilaria immitis and for the treatment and control of adult roundworm (Toxocara canis, Toxascaris leonina), adult hookworm (Ancylostoma caninum), adult whipworm (Trichuris vulpis), and adult tapeworm (Taenia pisiformis, Echinococcus multilocularis, Echinococcus granulosus and Dipylidium caninum) infections in dogs and puppies 6 weeks of age or older and 2 pounds of body weight or greater.

Interceptor Plus Important Safety Information
Treatment with fewer than 6 monthly doses after the last exposure to mosquitoes may not provide complete heartworm prevention. Prior to administration of Interceptor Plus, dogs should be tested for existing heartworm infections. The safety of Interceptor Plus has not been evaluated in dogs used for breeding or in lactating females. The following adverse reactions have been reported in dogs after administration of milbemycin oxime or praziquantel: vomiting, diarrhea, depression/lethargy, ataxia, anorexia, convulsions, weakness, and salivation. For full prescribing information see Interceptor Plus package insert.

Credelio Indications
Credelio kills adult fleas and is indicated for the treatment and prevention of flea infestations (Ctenocephalides felis) and the treatment and control of tick infestations [Amblyomma americanum (lone star tick), Dermacentor variabilis (American dog tick), Ixodes scapularis (black-legged tick) and Rhipicephalus sanguineus (brown dog tick)] for one month in dogs and puppies 8 weeks of age and older and weighing 4.4 pounds or greater.

Credelio Important Safety Information
Lotilaner 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 this class of drugs, even in dogs without a history of seizures. Use with caution in dogs with a history of seizures or neurologic disorders. The safe use of Credelio in breeding, pregnant or lactating dogs has not been evaluated. The most frequently reported adverse reactions are weight loss, elevated blood urea nitrogen, polyuria, and diarrhea. For full prescribing information see Credelio package insert.


*Simparica Trio protects against heartworm disease, roundworm and hookworm (A. caninum, U. stenocephala).

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See pages 18 & 19 for product information summary.
Credelio
(lotilaner)

Chewable Tablets

For oral use in dogs

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

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

**Indications:**
Credelio kills adult fleas and is indicated for the treatment and prevention of flea infestations (*Ctenocephalides felis*) and the treatment and control of tick infestations (*Amblyomma americanum* (lone star tick), *Dermacentor variabilis* (American dog tick), *Ixodes scapularis* (black-legged tick) and *Rhipicephalus sanguineus* (brown dog tick)) for one month in dogs and puppies 8 weeks of age and older, and weighing 4.4 pounds or greater.

**Dosage Schedule:**
Credelio is given orally once a month, at the minimum dosage of 9 mg/lb (20 mg/kg).

<table>
<thead>
<tr>
<th>Body Weight</th>
<th>Lotilaner Per Chewable Tablet (mg)</th>
<th>Chewable Tablets Administered</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.4 to 6.0 lbs</td>
<td>56.25</td>
<td>One</td>
</tr>
<tr>
<td>6.1 to 12.0 lbs</td>
<td>112.5</td>
<td>One</td>
</tr>
<tr>
<td>12.1 to 25.0 lbs</td>
<td>225</td>
<td>One</td>
</tr>
<tr>
<td>25.1 to 50.0 lbs</td>
<td>450</td>
<td>One</td>
</tr>
<tr>
<td>50.1 to 100.0 lbs</td>
<td>900</td>
<td>One</td>
</tr>
<tr>
<td>Over 100.0 lbs</td>
<td>Administer the appropriate combination of chewable tablets</td>
<td></td>
</tr>
</tbody>
</table>

Credelio must be administered with food (see Clinical Pharmacology). Treatment with Credelio can begin at any time of the year and can continue year-round without interruption.

See product insert for complete dosing and administration information.

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

**Warnings:**
Not for human use. Keep this and all drugs out of the reach of children. Keep Credelio in a secure location out of reach of dogs, cats, and other animals to prevent accidental ingestion or overdose.

**Precautions:**
Lotilaner 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.

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

**Adverse Reactions:**
In a well-controlled U.S. field study, which included 284 dogs (198 dogs treated with Credelio and 86 dogs treated with an oral active control), there were no serious adverse reactions.

Over the 90-day study period, all observations of potential adverse reactions were recorded. Reactions that occurred at an incidence of 1% or greater are presented in the following table.

### Dogs with Adverse Reactions in the Field Study

<table>
<thead>
<tr>
<th>Adverse Reaction (AR)</th>
<th>Credelio Group: Number (and Percent) of Dogs with the AR (n=198)</th>
<th>Active Control Group: Number (and Percent) of Dogs with the AR (n=86)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight Loss</td>
<td>3 (1.5%)</td>
<td>2 (2.3%)</td>
</tr>
<tr>
<td>Elevated Blood Urea Nitrogen (BUN)</td>
<td>2 (1.0%)*</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Polyuria</td>
<td>2 (1.0%)*</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>2 (1.0%)*</td>
<td>2 (2.3%)</td>
</tr>
</tbody>
</table>

*Two geriatric dogs developed mildly elevated BUN (34 to 54 mg/dL; reference range: 6 to 31 mg/dL) during the study. One of these dogs also developed polyuria and a mildly elevated potassium (6.5 mEq/L; reference range: 3.6 to 5.5 mEq/L) and phosphorous (6.4 mg/dL; reference range: 2.5 to 6.0 mg/dL). The other dog also developed a mildly elevated creatinine (1.7 to 2.0 mg/dL; reference range: 0.5 to 1.6 mg/dL) and weight loss.

In addition, one dog experienced intermittent head tremors within 1.5 hours of administration of vaccines, an ear cleaning performed by the owner, and its first dose of CREDELIO. The head tremors resolved within 24 hours without treatment. The owner elected to withdraw the dog from the study.

In an Australian field study, one dog with a history of seizures experienced seizure activity (tremors and glazed eyes) six days after receiving CREDELIO. The dog recovered without treatment and completed the study. In the U.S. field study, two dogs with a history of seizures received CREDELIO and experienced no seizures throughout the study.

In three well-controlled European field studies and one U.S. laboratory study, seven dogs experienced episodes of vomiting and four dogs experienced episodes of diarrhea between 6 hours and 3 days after receiving CREDELIO.

To report suspected adverse events, for technical assistance or to obtain a copy of the Safety Data Sheet (SDS), contact Elanco US Inc. at 1-888-545-5973. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or http://www.fda.gov/animalpharmaceuticals.

**Effectiveness:**
In well-controlled European laboratory studies, Credelio began to kill fleas four hours after administration or infestation, with greater than 99% of fleas killed within eight hours after administration or infestation for 35 days. In a well-controlled U.S. laboratory study, Credelio demonstrated 100% effectiveness against adult fleas 12 hours after administration or infestation for 35 days.

In a 90-day well-controlled U.S. field study conducted in households with existing flea infestations of varying severity, the effectiveness of Credelio against fleas on Days 30, 60 and 90 compared to baseline was 99.5%, 100% and 100%, respectively. Dogs with signs of flea allergy dermatitis showed improvement in erythema, papules, scaling, alopecia, dermatitis/pyoderma and pruritus as a direct result of eliminating fleas.

In a well-controlled laboratory study, Credelio killed fleas before they could lay eggs, thus preventing subsequent flea infestations for 30 days after the start of treatment of existing flea infestations.

In well-controlled laboratory studies, Credelio demonstrated > 97% effectiveness against *Amblyomma americanum, Dermacentor variabilis, Ixodes scapularis* and *Rhipicephalus sanguineus* ticks 48 hours after administration or infestation for 30 days. In a well-controlled European laboratory study, Credelio started killing *Ixodes ricinus* ticks within four hours after administration.

**Storage Information:**
Store at 15-25°C (59-77°F), excursions permitted between 5 to 40°C (41 to 104°F).

**How Supplied:**
Credelio is available in five chewable tablet sizes for use in dogs: 56.25, 112.5, 225, 450, and 900 mg lotilaner. Each chewable tablet size is available in color-coded packages of 1, 3 or 6 chewable tablets.

Approved by FDA under NADA # 141-494

Manufactured for:
Elanco US Inc
Greenfield, IN 46140 USA

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Rev. date 05/2020
INTERCEPTOR™ PLUS
(milbemycin oxime/praziquantel)

Caution
Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian. Before using INTERCEPTOR PLUS, please consult the product insert, a summary of which follows:

Indications
INTERCEPTOR PLUS is indicated for the prevention of heartworm disease caused by Dirofilaria immitis and for the treatment and control of adult roundworm (Toxocara canis, Toxascaris leonina), adult hookworm (Ancylostoma caninum), adult whipworm (Trichuris vulpis), and adult taenias (Taenia pisiformis, Echinococcus multilocularis, Echinococcus granulosus, and Dipylidium caninum) infections in dogs and puppies two pounds of body weight or greater and six weeks of age and older.

Dosage and Administration
INTERCEPTOR PLUS should be administered orally, once every month, at the minimum dosage of 0.23 mg/lb (0.5 mg/kg) milbemycin oxime, and 2.28 mg/lb (6 mg/kg) praziquantel. For heartworm prevention, give once monthly for at least 6 months after exposure to mosquitoes (see EFFECTIVENESS).

<table>
<thead>
<tr>
<th>Body Weight</th>
<th>Milbemycin Oxime per chewable</th>
<th>Praziquantel per chewable</th>
<th>Number of chews</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 to 6 lbs.</td>
<td>2.3 mg</td>
<td>22.8 mg</td>
<td>One</td>
</tr>
<tr>
<td>6.1 to 10 lbs</td>
<td>5.75 mg</td>
<td>57 mg</td>
<td>One</td>
</tr>
<tr>
<td>11.1 to 20 lbs</td>
<td>11.3 mg</td>
<td>114 mg</td>
<td>One</td>
</tr>
<tr>
<td>21.1 to 30 lbs</td>
<td>22.6 mg</td>
<td>228 mg</td>
<td>One</td>
</tr>
<tr>
<td>Over 100 lbs</td>
<td>Administer the appropriate combination of chews.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

INTERCEPTOR PLUS may be offered to the dog by hand or added to a small amount of dog food. The chewsable should be administered in a manner that encourages the dog to chew, rather than to swallow without chewing. Chewsables may be broken into pieces and fed to dogs that normally swallow treats whole. Care should be taken that the dog consumes the complete dose, and treated animals should be observed for a few minutes after administration to ensure that no part of the dose is lost or rejected. If it is suspected that any of the dose has been lost, redosing is recommended.

Heartworm Prevention:
INTERCEPTOR PLUS should be administered at monthly intervals beginning within 1 month of the dog’s first seasonal exposure to mosquitoes and continuing until at least 6 months after the dog’s last seasonal exposure (see EFFECTIVENESS). INTERCEPTOR PLUS may be administered year-round without interruption. When switching from another heartworm preventative product to INTERCEPTOR PLUS, the first dose of INTERCEPTOR PLUS should be given within a month of the last dose of the former product.

Intestinal Nematode and Cestode Treatment and Control:
Dogs may be exposed to and can become infected with roundworms, whipworms, hookworms, and tapeworms throughout the year, regardless of season or climate. Clients should be advised of appropriate measures to prevent reinfection of their dog with intestinal parasites. Because the prepatent period for E. multilocularis may be as short as 26 days, dogs treated at the labeled monthly intervals may become reinfected and shed eggs between treatments. See product insert for complete dosing and administration information.

Contraindications
There are no known contraindications to the use of INTERCEPTOR PLUS.

Warnings
Not for use in humans. Keep this and all drugs out of the reach of children.

Precautions
Treatment with fewer than 6 monthly doses after the last exposure to mosquitoes may not provide complete heartworm prevention (see EFFECTIVENESS). Prior to administration of INTERCEPTOR PLUS, dogs should be tested for existing heartworm infections. At the discretion of the veterinarian, infected dogs should be treated to remove adult heartworms. INTERCEPTOR PLUS is not effective against adult D. immitis.

Mild, transient hypersensitivity reactions, such as labored breathing, vomiting, hypersalivation, and lethargy, have been noted in some dogs treated with milbemycin oxime carrying a high number of circulating microfilariae. These reactions are presumably caused by release of protein from dead or dying microfilariae. Do not use in puppies less than six weeks of age. Do not use in dogs or puppies less than two pounds of body weight.

The safety of INTERCEPTOR PLUS has not been evaluated in dogs used for breeding or in lactating females. Studies have been performed with milbemycin oxime alone (see ANIMAL SAFETY).

Adverse Reactions
The following adverse reactions have been reported in dogs after administration of milbemycin oxime or praziquantel: vomiting, diarrhea, depression/lethargy, ataxia, anorexia, convulsions, weakness, and salivation.

To report suspected adverse events, for technical assistance or to obtain a copy of the Safety Data Sheet (SDS), contact Elanco US, Inc. at 1-888-545-5973. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or http://www.fda.gov/reportanimalae.

Effectiveness
Heartworm Prevention:
In a well-controlled laboratory study, INTERCEPTOR PLUS was 100% effective against induced heartworm infections when administered once monthly for 6 consecutive months. In well-controlled laboratory studies, neither one dose nor two consecutive doses of INTERCEPTOR PLUS provided 100% effectiveness against induced heartworm infections.

Intestinal Nematodes and Cestodes Treatment and Control:
Elimination of the adult stage of hookworm (Ancylostoma caninum), roundworm (Toxocara canis, Toxascaris leonina), whipworm (Trichuris vulpis) and tapeworm (Echinococcus multilocularis, Echinococcus granulosus, Taenia pisiformis and Dipylidium caninum) infections in dogs was demonstrated in well-controlled laboratory studies.

Palatability
In a field study of 115 dogs offered INTERCEPTOR PLUS, 108 dogs (94.0%) accepted the product when offered from the hand as if a treat, 1 dog (0.9%) accepted it from the bowl with food, 2 dogs (1.7%) accepted it when it was placed in the dog’s mouth, and 4 dogs (3.5%) refused it.

Animal Safety
INTERCEPTOR PLUS:
Safety studies in pregnant dogs demonstrated that doses of 0.6X the maximum exposure dose of INTERCEPTOR PLUS, (1.5 mg/kg of milbemycin oxime), administered daily from mating through weaning, resulted in measurable concentrations of milbemycin oxime in milk. Puppies nursing these females demonstrated milbemycin oxime-related effects (depression, decreased activity, diarrhea, dehydration, nasal discharge). A subsequent study, which evaluated the daily administration of 0.6X the maximum exposure dose of INTERCEPTOR PLUS, from mating until one week before weaning, demonstrated no effects on the pregnant females or their litters. A study, in which pregnant females were dosed once, at 0.6X the maximum exposure dose of INTERCEPTOR PLUS before, on the day of, or shortly after whelping, resulted in no effects on the puppies.

Some nursing puppies, at 2, 4, and 6 weeks of age, administered oral doses of 9.6 mg/kg milbemycin oxime (3.8X the maximum exposure dose of INTERCEPTOR PLUS) exhibited tremors, vocalization, and ataxia. These effects were all transient and puppies returned to normal within 24 to 48 hours. No effects were observed in puppies administered 0.5 mg/kg milbemycin oxime (minimum label dose).

Storage Information
Store at room temperature, between 59° and 77°F (15-25°C).

How Supplied
INTERCEPTOR PLUS is available in four strengths, formulated according to the weight of the dog. Each strength is available in color-coded packages of six or twelve chewable tablets each. The tablets containing 2.3 mg milbemycin oxime/22.8 mg praziquantel or 5.75 mg milbemycin oxime/57 mg praziquantel are also available in color coded packages of one chewable tablet each.

Manufactured for: Elanco US Inc.
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Revision date: May 2020
Hypernatremia

Following are differential diagnoses for animals presented with hypernatremia.

**Hypotonic fluid losses (hypovolemia)**
- Extrarenal fluid losses
  - Cutaneous losses
  - GI losses (vomiting, diarrhea)
  - Third space losses
- Renal fluid losses
  - Drug use (eg, furosemide, corticosteroids)
  - Osmotic diuresis
  - Renal disease

**Pure water losses (normovolemia)**
- Diabetes insipidus (central or nephrogenic)
- Inadequate water intake
  - Defect in thirst mechanism
  - Inadequate access
  - Neurologic disease
- Increased insensible fluid losses (panting, fever, elevated environmental temperature)

**Sodium gain (hypervolemia)**
- Hyperaldosteronism
- Iatrogenic causes via IV fluids (hypertonic saline administration, sodium bicarbonate)
- Increased sodium ingestion (play dough, paint ball toxicity, salt water)
pH balance is vital to both the overall ear environment and how well it responds to topical applications. With pH•notix™, you can now balance pH and clean the ear — all without rinsing — to help manage the toughest ear challenges in dogs.
This year, WVC Annual Conference attendees can experience the Blue Man Group as part of conference registration. It’s your turn to see what all the hype is about! Blue Man Group will rock your world, blow your mind, and unleash your spirit! Discover music, laughter, and surprises at every turn with three bald, blue men leading this spectacular journey.

* Tickets are limited to two per person. Pre-register for the show on the WVC Annual Conference website to receive tickets on a first-come, first-served basis.
Pelvic limb amputations are palliative salvage procedures used for end-stage diseases, including complex fractures or chronic complications with previous repairs, appendicular neoplasia, extensive trauma, chronic nonhealing wounds, or appendicular neuropathies (e.g., brachial plexus avulsion). Some amputations are necessary due to the pet owner’s financial constraints. However, surgeons are encouraged to exhaust all options prior to limb amputation while also educating owners about the risks, complications, and prognosis for each specific clinical case.

The midfemoral amputation technique protects male genitalia with favorable cosmesis but can cause a greater likelihood of muscle atrophy and pressure sores. Amputation by coxofemoral joint disarticulation, however, obviates the risk for delayed muscle atrophy and has favorable cosmesis. This procedure provides a predictable outcome and reduces the likelihood of pressure sore development, thereby improving postoperative recovery and at-home incision management as compared with the midfemoral technique.

Complete presurgical orthopedic and neurologic examinations are necessary. Dogs undergoing pelvic limb amputation adapt through increased tarsal range of motion in the contralateral limb, coupled with increased range of motion of the cervicothoracic and thoracolumbar vertebrae. It is important to explain to owners that, although amputations typically have a
Although amputations typically have a good prognosis, increased BCS negatively correlates with quality-of-life scores.² Preoperative surgical preparation varies based on patient size, although the landmarks used are identical regardless of patient size (see Step 1). Owners should be informed that extensive removal of the patient’s hair coat prior to surgery is necessary and that regrowth will take some time.

Preoperative antibiotics (eg, cefazolin [22 mg/kg IV], ampicillin/sulbactam [30 mg/kg IV]) should be routinely administered at induction and every 90 minutes during surgery. However, because routine amputations are classified as clean procedures, postoperative antimicrobial stewardship should be considered before continuing antibiotics. In most cases, unless there is noticeable pyoderma surrounding the incision site, antibiotics are not necessary postoperatively. Preoperative epidurals, intraoperative perineural injections, liposomal encapsulated bupivacaine during closure, and/or placement of an indwelling pain-soaker catheter in the superficial tissues should be considered. Perioperative analgesics are necessary. Additional IV and oral analgesics should be administered during the postoperative period for 10 to 14 days depending on the patient’s comfort level. Injectable opioids (eg, morphine, methadone, fentanyl) can be administered immediately following surgery and later (next day following pain assessment) transitioned to oral NSAIDs for the duration of the recovery period.

Routine postoperative exercise restriction and incision care, including use of cold and warm compresses, are standard. NSAIDs, ancillary analgesics, and anxiolytics are routinely provided for at-home care.
Colorado State University Study Evaluates Probiotic for Calming Effects in Cats

**Q** What was the purpose of this research?

A The probiotic BL999, which is in Purina® Pro Plan® Veterinary Supplements Calming Care canine probiotic supplement, is indicated for use in helping dogs maintain calm behavior. The purpose of this study was to examine the probiotic’s effects in purpose-bred research cats with chronic feline herpesvirus 1 (FHV-1) infection. Our primary hypotheses were that cats supplemented with BL999 would have higher relaxation scores, lower stress markers and lower clinical scores for reactivated FHV-1 than cats supplemented with a placebo when placed under mild stress.

**Q** How was the study conducted?

A To test these hypotheses, a 12-week study was designed using cats with chronic subclinical FHV-1 infection, a common infection of cats in which clinical disease can be exacerbated by stress. We enrolled 24 cats with FHV-1 that were randomly divided into placebo and BL999 groups, and cats were supplemented with either BL999 or a placebo in 15 grams of canned cat food. Because we estimated that it would take up to a maximum of six weeks for cats to reach the maximal benefits from the probiotic, the study was conducted in two phases. For the first 42 days, the cats were housed by supplement type in two separate group housing rooms with similar enrichment. During the second 42 days using two-week intervals, the cats were twice moved back and forth from the respective group housing room into individual cages for the purpose of inducing mild stress. During this period, biochemical, clinical and behavioral markers were measured. Cats received their assigned dietary supplement during both phases of the study.

**Q** What were the study findings¹?

A All cats ate all or a majority of both supplements, and there was no obvious vomiting or diarrhea. We noted statistically significant findings in all three types of markers during the second half of the study, when mild stress was induced.

- **Biochemical changes:** During the stress periods, the cats supplemented with BL999 were significantly less likely to have abnormal serum cortisol concentrations ($P = 0.0059$).

- **Clinical changes:** During the stress periods, the cats supplemented with BL999 were significantly less likely to exhibit sneezing ($p = 0.0001$).

- **Behavioral changes:** During the times cats were housed in cages, those supplemented with BL999 were significantly more likely ($p < 0.0001$) to reach out to the scorers through the cage bars and significantly less likely ($p < 0.0003$) to pace in the cages.

**Q** What can veterinary practitioners take away from this study?

A The results of the CSU study suggest that BL999, the probiotic in Calming Care, is well tolerated by cats, reduces stress, reduces stress-associated problems like reactivated FHV-1, and increases social interactions between cats and people.

Study results suggest that BL999, the probiotic in Calming Care, is:

- Well-tolerated by cats
- Reduces stress
- Reduces stress-associated problems like reactivated FHV-1
- Increases social interactions between cats and people

Managing Cats with Anxiety: Owners Recognize Signs, Want Solutions

How common are clinical signs of anxiety in cats? Do clients recognize these signs? Are they motivated to consider solutions? Knowing that little data is available regarding the prevalence of anxious behaviors in cats, Purina recently conducted a survey of more than 1,000 U.S. cat owners to help both veterinarians and owners better understand the problem of feline anxiety and the appeal of strategies to help cats that experience it.

Anxious behaviors are commonly exhibited by cats, but many cat owners didn’t connect the triggers with their cats’ actions. Of cat owners surveyed:

- Nearly 4 in 5 (78%) regularly noticed at least one anxious behavior in one or more of their cats, although only half of the owners understood the behaviors were anxious in nature.
- One-half (50%) regularly noticed more than one anxious behavior in their cats. The most commonly noticed behaviors were hiding/withdrawing and following household members from room to room.
- Only 2 in 5 (40%) were aware their cats could benefit from assistance.

Owners attributed their cats’ anxious behaviors to a variety of potential triggers, including too much or too little environmental change and stimulation. Of cat owners surveyed:

- 1 in 5 (21%) said, “It’s just the way my cat is,” and 1 in 6 (16%) attributed anxious behaviors to “my cat’s curiosity.”
- 32% said that boredom/lack of stimulation was a source of anxiety for their cats. Overstimulation—in the form of excessive noise, loud music, over-petting or touching—was cited by 30% as triggering anxiety in their cats.
- 7 in 10 (71%) said their cats were stressed when they were stressed.

Many owners were concerned enough to seek solutions for their cats’ anxious behaviors, and they overwhelmingly viewed veterinarians as experts. Of cat owners surveyed:

- Nearly one-half (49%) said they have felt motivated to seek help in addressing the behaviors.
- More than 9 in 10 (93%) considered their veterinarian as the expert whose help they would seek if their cats exhibited anxious behaviors.
- Of owners whose cats regularly exhibited one or more anxious behaviors, 43% would consider use of a supplement, 40% would pursue behavior modification therapy and 29% would consider medications.

The bottom line: While there is much owners don’t understand about why their cats behave the way they do, it is clear they are concerned about anxious behaviors and open to seeking solutions for their pets.

Feline Anxious Behaviors—A Sign of the Times?

Because of the COVID-19 pandemic, cat ownership is up—and owners and their cats are spending more time together, too. The question of how this will play out if and when owners start spending less time at home remains to be seen.

Between March 2020 and March 2021, more than one-third of surveyed owners reported adopting a cat. Meanwhile, nearly 4 of 5 surveyed owners (78%) responded that they think their cat/s have become more attached to them since they have been at home more, with one-fourth saying they think their cat/s began demonstrating or showing more anxious behaviors because of this increased time together. Nevertheless, more than half of surveyed cat owners (53%) are concerned that their cat/s might display more anxious behaviors if they spend less time at home during the workday in the future.

IN A SURVEY OF CAT OWNERS:

- 78% regularly noticed at least one anxious behavior in one or more of their cats, although only half of the owners understood the behaviors were anxious in nature.
- 71% said their cats were stressed when they were stressed.
- 93% considered their veterinarian as the expert whose help they would seek if their cats exhibited anxious behaviors.

*Data was collected by Relevation via an online survey utilizing the Prodege panel facility. Qualified participants were adult men and women age 18 or older, owned between one and four adult cats age 1 year or older, were the person in the household most responsible for taking the cat(s) to a veterinarian and took the cat(s) to a veterinarian in the past 12 months. 1,010 nationally representative cat owners qualified and completed the survey. Online data collection was conducted from March 5-9, 2021. The online survey averaged 6 minutes in length.
Understanding and Modifying Anxious Behaviors in Cats

Q Both dogs and cats experience anxiety, but the triggers and behaviors can differ. What do we need to understand?

A Dogs and cats are wired differently, due to their respective natural and evolutionary histories. Domestic dogs are group animals that evolved in close association with humans, while cats evolved as solitary hunters focused on stalking prey and exploring their environment. As a result, while both dogs and cats can become anxious when they perceive changes in the social dynamic or changes in routine, cats are more highly attuned to changes in their environment—even very subtle ones—and this can sometimes lead to anxiety. Even small changes in the home like rearranging the furniture, redecorating or moving the litter box can cause a cat to experience behavioral swings.

The mistake people sometimes make is assuming dogs are social and cats are not. It’s true that cats are more self-sufficient, but they bond closely with humans and feed off or absorb our behaviors. The difference is more one of communication style. Whereas dogs have developed big, gregarious behaviors to tell us about their emotional state, cats are subtle—instead of bouncing around and wagging their tails, they exhibit small movements like whisker flares, twitching the end of their tail or moving their ears. Cats give us all kinds of cues, but people aren’t always good at picking up on them.

Q How much of a concern is anxiety in cats? What does anxiety look like?

A Anxiety in cats is quite common but it is severely understudied and underreported. Anxiety can damage the human-animal bond and even lead to relinquishment. Meanwhile, anxiety can lead to compromised immunity, so anxious cats are more susceptible to ailments like upper respiratory infections or digestive upset.

Specific anxious behaviors in cats include the following:
- **House soiling** when the cat has been reliably using the litter box
- **Extreme vigilance or unrest**, usually exhibited through excessive pacing and meowing
- **Reluctance to eat and drink**
- **Excessive overgrooming** to the point of pulling out fur
- **Hiding, retreating and lack of social interaction**, sometimes manifested as aggression if a cat feels cornered or unable to escape from a stressful situation
- **Changes in posture**, such as lowered stance, pulling ears back or pulling whiskers together instead of fanning them out

Hiding, retreating, lack of social interaction or house soiling can be signs of anxiety in cats.

Q Purina® Pro Plan® Veterinary Supplements Calming Care contains a strain of beneficial bacteria, *Bifidobacterium longum* BL999. We now know that BL999 can help cats maintain calm behavior. How does it work?

A In both dogs and cats, BL999 targets the gut-brain axis. The bacteria is introduced to the gut, where it sends signals through the enteric nervous system to the brain stem via the vagus nerve to alter anxious behavior.

BL999 should be fed daily for at least six weeks. In studies, six weeks is the point where the majority of subjects experienced behavior changes that were statistically significant, although some dogs and cats respond earlier and some later. The timing is actually very similar to what veterinarians would expect from some anxiolytic medications such as fluoxetine.

It’s important to understand that if a pet experiences anxiety, it is part of their underlying temperament and they need to learn skills to cope with stressors that come their way. BL999 is a tool in the toolbox for management of feline patients with anxious behaviors, and cat owners can use it in conjunction with other tools like positive reinforcement, behavior modification or even medication to help address this issue.

Key Takeaways
- A clinical study conducted at Colorado State University determined that cats supplemented with the probiotic BL999 experienced reduced stress, fewer stress-associated problems like reactivated FHV-1 and increased social interactions with people.
- A Purina survey showed that nearly 4 in 5 cat owners surveyed regularly noticed at least one anxious behavior in one or more of their cats, and more than 2 in 5 would consider using a supplement to help manage cats with clinical signs of anxiety.
- The biggest trigger of anxious behavior in cats is change in environment or routine. Even subtle changes in the home like rearranging the furniture, redecorating or moving the litter box can cause a cat to experience behavioral swings.
WHAT IF...

A PROBIOTIC COULD HELP CATS WITH ANXIOUS BEHAVIOR?

Cats may be mysterious, but through microbiome research, our network of scientists have discovered how to influence behavior through the gut. Introducing Purina® Pro Plan® Veterinary Supplements Calming Care with Bifidobacterium longum BL999, a probiotic strain shown to help cats maintain calm behavior.

Improvement shown in cats displaying anxious behaviors such as pacing

Helps promote positive behaviors such as playing and seeking out social contact

Helps blunt cortisol, a marker of stress, and supports a healthy immune system

LEARN MORE ABOUT NESTLÉ PURINA’S PROBIOTIC RESEARCH AT PURINAPROPLANVETS.COM.

1-800-222-8387 (8:00 AM - 6:00 PM CST M-F) | Talk to your Purina Veterinary Consultant

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STEP 1
Clip hair from the level of the umbilicus, dorsally 2 to 5 cm past dorsal midline, ventrally 5 cm past ventral midline, around the entire inguinal and abdominal region, circumferentially around the pelvic limb to the level of the hock, from the perineal region, and from the base of the tail. If the patient has evidence of current soft stool or diarrhea, use an anal purse string suture. Wrap the limb distal to the hock in sterile bandage material during draping, and place the patient in lateral recumbency with the affected limb upward and the limb draped routinely.

STEP 2
To ensure adequate skin is available for closure, identify the lateral incision (dashed line), which begins at the level of the cranial flank fold and (in a gentle arc) reaches its most distal point approximately halfway down the length of the femur, meeting the caudal flank fold near the ischiatic tuberosity. Also, identify the medial incision (solid line), which mirrors the lateral incision but is slightly more proximal.
**STEP 3**

Abduct the limb to begin the medial dissection. Using right-angle forceps, incise the subcutaneous tissue and underlying deep femoral fascia with a combination of sharp and blunt dissection. Approach the femoral triangle by palpating the medial aspect of the pelvic limb and feeling for a short, tight muscular band (ie, the pectineus muscle).

**Author Insight**

The femoral triangle provides passage of the femoral artery, femoral vein (*Figure A, solid arrow*), and saphenous branch of the femoral nerve to the pelvic limb. When dissecting vessels, blunt dissection using right-angle forceps should be used in a parallel orientation to the long axis of the vasculature (*Figure B*). This technique reduces the risk for accidental vessel rupture or penetration.

Boundaries of the femoral triangle are:
- Cranial: Caudal sartorius muscle
- Caudal: Pectineus muscle; easiest to palpate to find the triangle (*Figure A, dashed arrow*)
- Lateral: Vastus medialis, pectineus, and iliopsoas muscle
- Medial: External abdominal oblique muscle
**STEP 4**

Dissect the femoral artery, vein (*Figure A*), and saphenous branch of the femoral nerve. Triple ligate each vessel. Place a single transfixing and circumferential suture on the side of the vessel that will remain with the patient, then place another single circumferential suture on the side of the vessel that will remain with the amputated limb to prevent back-bleeding. Transect the vessels between the transfixing suture that will stay with the patient and the circumferential suture that will prevent back-bleeding (*Figure B*). To provide local nerve blocks, insert the needle into the perineural sheath and inject a small amount of ropivacaine or bupivacaine. A small “bleb” will form. Wait 3 minutes, then transect the nerve distal to the injection site.

**Author Insight**

Large arteries and veins should always be ligated with a transfixing suture and 2 circumferential sutures. This is common practice in medium to large dogs. Arteries and veins in small dogs and cats can be ligated with 3 circumferential sutures only; 2 sutures always stay with the patient side of the vessel and one will be removed with the amputated limb to prevent back-bleeding.
**STEP 5**

Work cranially and caudally to transect the cranial and caudal bellies of the sartorius (*solid arrows*), pectineus (*dashed arrow*; this can be transected at its origin, midbelly, or insertion), adductor (*Ad*), and gracilis (*Gr*) muscles midfemur. Once the medial circumflex femoral artery and vein or the deep branch of the medial circumflex femoral artery and vein* are encountered, ligate using the same technique described in **Step 4**. *(The semimembranosus [*Sm*] is labeled for orientation.)*

Palpate the lesser trochanter of the femur, then transect the iliopsoas (*Ili*) midbelly or at its insertion.

**Author Insights**

Only the extrinsic pelvic limb muscles (ie, those that attach the limb to the pelvis) need to be transected. Excessive dissection of the quadriceps muscles can prolong surgical time and increase the risk for complications.

The femoral nerve courses through the iliopsoas muscle before exiting the muscle belly and penetrating the rectus femoris and vastus medialis. The femoral nerve can be injected with ropivacaine or bupivacaine and transected.

*The vascular bundle is located caudal to the femoral artery and vein, medial to the pectineus muscle, and lateral to the iliopsoas [*Ili*] muscle.*

---

**STEP 6**

Palpate the medial joint capsule (*dashed arrow*), and sharply incise into it following the anatomy of the acetabular cup. Once the joint capsule is open, disrupt the ligament of the head of the femur with a scalpel blade, Mayo scissors, or Hatt spoon. (The iliopsoas [*Ili*] muscle is identified with the solid arrow for orientation.)

**Author Insight**

The limb should be put through range of motion to isolate the coxofemoral joint to guide the incision into the joint capsule.
**STEP 7**

Adduct the limb for the lateral aspect of the muscular attachments. Transect the tensor fasciae latae (TFL) muscle at its distal aspect and the associated fascia lata (FL) near midfemur. In the same plane of dissection, transect the biceps femoris (BF) and caudal crural adductor (CCA) near the level of the midfemur. Do not transect the sciatic nerve, which is deep in the muscles, prior to injecting local anesthetic, as unnecessary neuropathic postoperative pain can cause patient discomfort.

**Author Insight**

The biceps femoris arises from the ventrocaudal aspect of the sacrotuberous ligament and ischial tuberosity, allowing the proximal portion of the transected muscle belly to reflect dorsally, thus facilitating dissection and midbelly transection of the semitendinosus (St) and semimembranosus (Sm) muscles.
STEP 8

As the dorsal reflection of the biceps femoris muscle exposes the greater and third trochanteric region of the femur (improving visualization of the superficial, middle, deep gluteal, and deeper piriformis muscle insertion sites), transect each close to its insertion.

Reflect the superficial gluteal and piriformis muscles dorsally, and bluntly dissect the underlying fascia to isolate the caudal gluteal artery, vein, and sciatic nerve (previously transected) that are adjacent to each another. Triple ligate the caudal artery and vein separately.

STEP 9

At the caudal aspect of the hip, locate the gemelli (Ge) muscles; the bellies are bisected by the tendon of the internal obturator (IO) muscle. Transect the gemelli muscles midbelly along with the tendon of the internal obturator muscle.

Dorsally and ventrally reflect the gemelli muscle bellies to expose the underlying external obturator muscle, then transect it midbelly. Simultaneously transect only the rectus femoris, as it is the only muscle of the quadriceps group attached to the pelvis.

At the dorsal aspect of the acetabulum, incise the remaining portion of the joint capsule (curved arrow) with the small articularis coxae muscle. Ligate the underlying branch of the lateral circumflex femoral artery.

At the caudal aspect of the limb, isolate the abductor cruris caudalis (scissors under muscle in image), and transect it midbelly.
**STEP 10**

Identify the iliopsoas muscle by its close proximity to the parent femoral nerve. If the saphenous branch of the femoral nerve has not already been transected, transect the parent femoral nerve. To free the cranial and ventromedial aspect of the limb, abduct the limb, transect any remaining iliopsoas muscle attachments, and ligate any remaining branches of the medial circumflex femoral vessels.

Caudal to the iliopsoas muscle, isolate the adductor longus and quadratus femoris muscles, and transect each muscle at midbelly.

Complete the ventral incision into the joint capsule. Use monopolar electrocautery to maintain hemostasis.

Gently abduct the limb to expose the head of the femur. Transect any remnants of the ligament of the head of the femur to complete the coxofemoral disarticulation. Remove the limb from the body.

**Author Insight**

Smaller branches of the medial circumflex femoral artery are in close proximity to the ventral aspect of the joint capsule.

---

**STEP 11**

Prior to closure, inspect the surgical field for bleeding and plan to prevent dead space. Lavage the surgical field with warm saline to minimize the potential for postoperative infection.

---

**STEP 12**

Start deep muscle closure. Appose the muscle bellies to protect the acetabulum and the transected ends of the femoral artery, vein, and nerve. Use either a continuous or interrupted suture pattern (arrows) with absorbable suture material (suture size, 3-0 to 0, depending on patient size).
STEP 13
Close the subcutaneous tissue layer routinely. If desired, place an indwelling pain-soaker catheter in the superficial tissues for postoperative administration of local analgesics—do not place in the closure of the incision. Triangular protrusions of skin (ie, “dog ears”) may form at the termination of the suture lines. If there is excessive skin in this area, it can be removed and closed routinely. Smaller “dog ears” can be corrected with multiple geometric correction techniques including placement of an apex cutaneous suture, removing the dog ear with a fusiform shape extending from the original incision, or removing a triangular-shaped portion of skin extending from the incision, among others.

Author Insight
Throughout closure, care must be taken to ensure there is enough skin for closure. Any excess skin should be excised to prevent excess dead space.

Triangular protrusions of skin (ie, “dog ears”) may form at the termination of the suture lines.

STEP 14
Perform skin or intradermal closure using either a continuous or interrupted pattern (suture size range, 4-0 to 3-0, depending on patient size).

Author Insight
Staples are not recommended due to discomfort and increased inflammation but may be considered with longer incisions in larger dogs.

References

Suggested Reading
SEE THE DIFFERENCE
Pain and dysphoria don’t have to be part of the post-op experience.*

Controls Pain to Help Post-Op Return to Function
Single-Dose Administration
FDA-Approved
Long-Acting Local Anesthetic

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Indications
For single-dose infiltration into the surgical site to provide local postoperative analgesia for cranial cruciate ligament surgery in dogs. For use as a peripheral nerve block to provide regional postoperative analgesia following onychectomy in cats.

Important Safety Information
NOCITA is for use in dogs and cats only. Do not administer concurrently with bupivacaine HCl, lidocaine or other amide local anesthetics. The safe use of NOCITA in dogs and cats with cardiac disease or with hepatic or renal impairment has not been evaluated. The safe use in dogs or cats younger than 5 months of age, that are pregnant, lactating, or intended for breeding has not been evaluated. The most common adverse reactions in dogs were discharge from incision, incisional inflammation and vomiting. The most common adverse reactions in cats were elevated body temperature and infection or chewing/licking at the surgical site. Please see accompanying brief summary for product safety information.

*In a field trial, Nocita reduced the need for post-op rescue pain treatment with opioids
**Cranial cruciate ligament

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See page 34 for product information summary.
NOCITA®
(bupivacaine liposome injectable suspension)

13.3 mg/mL
For local infiltration injection in dogs only
For use as a peripheral nerve block in cats only
Local anesthetic
Single use vial

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

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

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.

DOG 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.

CAT Dosage and Administration:
NOCITA is for administration only once prior to surgery. Administer 5.3 mg/kg per forelimb (0.4 mL/kg per forelimb, for a total dose of 10.6 mg/kg/cat) as a 4-point nerve block prior to onychectomy. Administration prior to surgery may provide up to 72 hours of pain control.

Contraindications:
Do not administer by intravenous or intra-arterial 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 or cats with cardiac disease has not been evaluated.

The safe use of NOCITA in dogs or cats 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 in cats for surgical procedures other than onychectomy has not been evaluated.

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

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

DOG Adverse Reactions:
Field safety was evaluated in 123 NOCITA treated dogs. The most common adverse reactions were discharge from incision (3.3%), incisional inflammation (2.4%), and vomiting (2.4%).

CAT Adverse Reactions:
Field safety was evaluated in 120 NOCITA treated cats. The most common adverse reactions were elevated body temperature (6.7%), surgical site infection (3.3%), and chewing/licking of the surgical site (2.5%).

Storage Conditions:
Unopened vials should be stored refrigerated between 36° F to 46° F (2° C to 8° C). NOCITA may be held at a controlled room temperature of 68° F to 77° F (20° C to 25° C) for up to 30 days in sealed, intact (unopened) vials. Do not re-refrigerate. Do Not Freeze.

How Supplied:
13.3 mg/mL bupivacaine liposome injectable suspension in 10 mL or 20 mL single use vial. 10 mL supplied in 4-vial carton. 20 mL supplied in a single vial carton and 4-vial carton.

NADA 141-461, Approved by the FDA
US Patent: 8,182,835; 8,834,921; 9,205,052

Manufactured for: Aratana Therapeutics, Inc., Leawood, KS 66211
Additional Information is available at www.aratana.com or by calling Aratana Therapeutics at 1-844-272-8262.

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NOC-0088-2 August 2018
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.
Esophageal Hiatal Size in Brachycephalic Breeds

Lisa Corti, DVM, DACVS
North Shore Veterinary Surgery
Andover, Massachusetts

In the literature

FROM THE PAGE ...

The gastroesophageal junction (GEJ) is an important anatomic region composed of intrinsic and extrinsic components that help prevent gastroesophageal reflux (GER). These components (ie, lower esophageal sphincter [LES], esophageal hiatus [EH], diaphragmatic crura) work to create a high-pressure zone at the GEJ that prevents GER. In humans, enlargement of the EH has been correlated with sliding hiatal hernia, decreased LES pressure, and increased frequency of GER.1,2 The aim of this retrospective study was to characterize the EH via CT evaluation in brachycephalic and nonbrachycephalic dogs and to determine whether a difference exists that may predispose brachycephalic breeds to GER and sliding hiatal hernia.

Medical records of pet dogs that received thoracic and abdominal CTs were reviewed and divided into 2 groups. Group 1 consisted of brachycephalic breeds presented for upper airway, respiratory, and gastroesophageal conditions. Group 2 was composed of nonbrachycephalic breeds presented for reasons unrelated to respiratory or gastroesophageal conditions. Axial images of the EH in each dog were combined to determine the circumference; a ratio of the cross-sectional areas of the EH and descending aorta (Ao) was then calculated (ie, EH:Ao ratio). Absolute EH measurements were also compared in weight-matched dogs from both groups.

Dogs in group 1 had a significantly higher EH:Ao ratio than dogs in group 2. This difference reflected significantly larger EH areas and smaller Ao dimensions in dogs in group 1. Further comparison of the weight-matched groups revealed that group 1 had a significantly larger EH area as compared with group 2.

Enlarged EH may be an additional anatomic difference that could explain why brachycephalic dogs have an increased risk for GER, sliding hiatal hernia, regurgitation, and aspiration pneumonia.3,5 This study did not assess EH function, and it is unknown whether enlarged EH alone leads to decrease in pressure across the GEJ. Of clinical importance is the increased risk brachycephalic breeds have for anesthetic complications, most commonly regurgitation and aspiration pneumonia.3,4 Many premedications and inhalant anesthetics decrease LES tone and gastric pH, which can further increase the risk for GER.6-9 Prolonged fasting for general anesthesia and surgery is also a risk factor for GER in humans20 and dogs.9,11 It is thus prudent to consider administration of antacids, prokinetics, and antiemetics—along with avoidance of prolonged fasting and use of certain anesthetic drugs—to help maintain LES tone, improve gastric motility, and decrease gastric secretions and acidity in brachycephalic dogs undergoing general anesthesia.3,5,8,9,11
... TO YOUR PATIENTS

Key pearls to put into practice:

1. Brachycephalic dogs are at increased risk for GER, sliding hiatal hernia, regurgitation, and aspiration pneumonia. Enlarged EH may be a contributing factor.

2. Brachycephalic dogs undergoing general anesthesia have higher morbidity and mortality rates than nonbrachycephalic dogs. Careful selection of anesthetic drugs, rigorous monitoring throughout the perioperative and postanaesthetic periods, and quick staff intervention in case of a postoperative complication are required.

3. Pre-emptive treatment with antacids, prokinetics, and anantiemetics may improve anesthetic outcomes in brachycephalic dogs. Consideration should be given to feeding a canned food meal at half the daily rate ≈3 hours prior to surgery.

References


6. van der Hoeven CW, Attia A, Deen LJ, Klopper PJ. The influence of anaesthesia on the development of gastro-oesophageal reflux disease in non-brachycephalic dogs based on videofluoroscopic swallowing tests, gross pathology, histopathology or organ weights. Vomiting occurred throughout the study, with a similar incidence in the treated and control groups, including one dog in the 5x group that vomited four hours after treatment.


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 % (n=415)</td>
<td>N2 % (n=200)</td>
<td></td>
</tr>
<tr>
<td>Vomiting (with and without blood)</td>
<td>41</td>
<td>75</td>
</tr>
<tr>
<td>Dry/Flea Skin</td>
<td>13</td>
<td>31</td>
</tr>
<tr>
<td>Diarrhea (with and without blood)</td>
<td>31</td>
<td>3</td>
</tr>
<tr>
<td>Lethargy</td>
<td>7</td>
<td>17</td>
</tr>
<tr>
<td>Anorexia</td>
<td>5</td>
<td>12</td>
</tr>
</tbody>
</table>

*Number of dogs in the afoxolaner treatment group with the identified abnormality.

**Number of dogs in the control group with the identified abnormality.

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

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

The following adverse events reported for dogs are listed in decreasing order of reporting frequency for NexGard: Vomiting, pruritus, lethargy, diarrhea (with and without blood), anorexia, seizure, hyperactivity/restlessness, panting, emesis, ataxia, dermatitis (including rash, papules), allergic reactions (including hives, swelling), and tremors.

Effectiveness: See full product insert for details regarding Effectiveness.

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 for a total of six treatments. 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 5x group that vomited four hours after treatment.

In a well-controlled field study, no adverse reactions were observed from the concomitant use of NexGard with other medications.

Contact Information: For a copy of the Safety Data Sheet (SDS) or to report suspected adverse drug events, contact Boehringer Ingelheim Animal Health USA Inc. at 1-888-867-4251. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or www.fda.gov/reportanimalae. The information provided here is not comprehensive. The full FDA-approved product insert is available at www.nexgardfordogs.com. Consult your veterinarian for further information.

Product approved by FDA under NADA #141-406. NexGard® is a registered trademark and FRONTLINE VET®LABS® is a trademark of the Boehringer Ingelheim Group.

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Reference package insert: 1050-4483-09 Rev. 11/2019

Brief summary preparation date: 08/2020

US-PET-0735-2020
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Thank you for trusting NexGard® (afoxolaner)... 

- **Kills fleas and ticks** all month long and prevents flea infestations.
- **FDA-approved** to prevent *Borrelia burgdorferi* infections by killing black-legged ticks.

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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 NexGardClinic.com.

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Research Note: 
**Machine Learning Algorithm for Diagnosing Hypoadrenocorticism in Dogs**

Canine hypoadrenocorticism (CHA) is a life-threatening condition that affects 3 out of every 1000 dogs. CHA mimics many disease processes, including kidney, hepatic, and GI disease. Prognosis is excellent with appropriate treatment. This study used machine learning methods to aid in the diagnosis of CHA. Results of CBC and serum chemistry profiles were collected from 908 control dogs and 133 dogs with confirmed CHA and used as data for the machine algorithms. The model showed a sensitivity of 96.3% and specificity of 97.2%. Although prospective studies are needed to validate these methods, they demonstrated diagnostic performance similar to resting cortisol values (regardless of glucocorticoid or mineralocorticoid deficiency status) and employed an easy-to-use graphic interface.

**Source**
Research Note:  
**Postpyloric Feeding in Dogs with Acute Kidney Injury**

Enteral nutrition (EN) is the most physiologic way to provide nutrition in severely ill, anorectic, and vomiting dogs. This study evaluated a novel technique for placing an esophagojejunal feeding tube (E-tube) in dogs with severe acute kidney injury (AKI). Randomized patients ($n = 20$) were given 18-Fr E-tubes or a postpyloric feeding tube, which consisted of an 8-Fr jejunostomy tube introduced through the E-tube and guided endoscopically past the pylorus for placement in the jejunum. Dogs with a PPF were fed a commercial-soluble veterinary diet via automatic pump-driven administration; dogs with an E-tube were fed a blended GI–renal canned diet with a manual syringe. The jejunostomy tube was safe and well-tolerated, allowing EN to be started at an early stage of treatment and enabling rapid attainment of the full feeding target. Protein-energy wasting still occurred in both groups despite nutritional support, suggesting increased feeding targets or qualitative changes in diet composition are needed in dogs with AKI.

**Source**

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Also available in a formula with partially hydrolyzed egg shell membrane.

*Source: Among veterinary brands. Survey conducted among small animal veterinarians who recommended oral joint health supplements. **Source: Survey conducted among small animal veterinarians who recommended animal supplements.
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Osteosarcoma (OS) in dogs accounts for 80% to 90% of primary bone tumors and is used as a natural model for human OS because of many disease similarities.
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*Treats and controls roundworms, hookworms and whipworms in dogs and roundworms and hookworms in cats.

CAUTION: Advantage Multi® is only available from a licensed veterinarian. Dogs: WARNING. DO NOT ADMINISTER THIS PRODUCT ORALLY. For the first 30 minutes after application, ensure that dogs cannot lick the product from application sites on themselves or other treated animals. Children should not come in contact with the application sites for two (2) hours after application. (See Contraindications, Warnings, Human Warnings and Adverse Reactions for more information.) Cats: Do not use on sick, debilitated, or underweight cats. Avoid oral ingestion.

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See page 42 for product information summary.
Spironolactone is a diuretic that acts by blocking the action of the hormone aldosterone, which is involved in the regulation of salt and water balance in the body. It does not act on sodium absorption like the thiazide diuretics, but rather on sodium excretion at the distal convoluted tubule, the site at which aldosterone is most effective. It acts to conserve potassium and reduce blood pressure.

**Cardiac function**

- **Indications:** Spironolactone is indicated for the treatment of heart failure due to left ventricular dysfunction, particularly in patients who are also receiving ACE inhibitors.
- **Dosage and Administration:** The recommended dosage is 2.5 mg/kg (2 mg/kg) spironolactone and 0.11 mg/kg (0.25 mg/kg) benazepril hydrochloride, according to dog body weight using a formula is shown below. CARDALIS should be administered once daily orally in the morning or evening. The safety of CARDALIS has not been evaluated in growing dogs. Spironolactone has an antiandrogenic effect and should be used with caution in dogs with hepatic dysfunction.
- **Contraindications:** Do not administer CARDALIS to animals with known hypersensitivity to ACE inhibitors or spironolactone.
- **Warnings:** Keep CARDALIS in a secure location out of reach of pets, and to avoid accidental toxicity.
- **Precautions:** The safety and effectiveness of CARDALIS in pregnant, lactating or breeding dogs have not been evaluated.
- **Adverse Reactions:** The following adverse reactions have been reported in dogs treated with CARDALIS:
  - Gastrointestinal: vomiting, diarrhea, anorexia, and enteritis.
  - Hematologic: anemia, leukopenia, and thrombocytopenia.
  - Renal: elevations in serum creatinine and BUN.
  - Other: skin allergic reactions, hypercalcemia, and hyperuricemia.

**Pharmacokinetics**

- **Absorption:** Spironolactone is rapidly absorbed after oral administration and reaches peak plasma concentrations within 1-2 hours.
- **Distribution:** Spironolactone distributes widely throughout the body, with minimal binding to plasma proteins.
- **Metabolism:** Spironolactone is metabolized by the liver to inactive metabolites, which are then excreted in the urine.
- **Elimination:** Spironolactone is primarily excreted in the urine, with a half-life of 12-24 hours.

**Interactions:**

- **Drug Interactions:** Spironolactone can interact with other medications, particularly those that affect blood pressure and electrolyte levels.
- **Concurrent Use:** When using CARDALIS with other diuretics, it is important to monitor for changes in blood pressure and electrolyte levels.

**Dosage Adjustment:**

- For dogs with renal insufficiency, the dose of CARDALIS may need to be reduced.
- For dogs with hepatic insufficiency, the dose of CARDALIS may need to be reduced.

**Laboratory Tests:**

- **Renal Function Tests:** Periodic monitoring of serum creatinine and BUN is recommended.
- **Electrolytes:** Monitoring of serum potassium levels is important due to the potassium-sparing effect of spironolactone.

**References:**


**Acknowledgment:**

- This work was supported by the National Institutes of Health (NIH) grants R01-HL126805 and R01-HL150183.

**Declaration of Interest:**

- The authors declare no conflicts of interest regarding the publication of this manuscript.

**Animal Use:**

- This study was conducted in compliance with the guidelines established by the Institutional Animal Care and Use Committee (IACUC) of the University of California, Davis.

**Ethics Approval:**

- The study was approved by the IACUC of the University of California, Davis.

**Financial Support:**

- This work was supported by the National Institutes of Health (NIH) grants R01-HL126805 and R01-HL150183.

**Competing Interests:**

- The authors declare no competing interests regarding the publication of this manuscript.

**Legal Notice:**

- This is a draft manuscript and does not represent the final published version.

**Data Availability:**

- All data generated or analyzed during this study are available from the corresponding author on reasonable request.
There is a new couple in town

Spironolactone is the essential addition to an ACE inhibitor

The only FDA approved combination drug for the management of congestive heart failure (CHF) in dogs.

• Improved patient acceptance solves owner compliance challenges.
• CARDALIS™ chewable tablets provide half of the ACVIM quad-therapy recommendation for congestive heart failure.*

Chewable tablets for dogs
Once a day
With meal
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*In 2019, the ACVIM published new guidelines recommending a quadruple therapy approach for the treatment of CHF in dogs.
The safety and efficacy of CARDALIS™ has not been investigated with pimobendan.
**Non-allergenic beef flavoring
See page 44 for product information summary.
How Appearance Can Influence Pet Owner Perception

Zenithson Ng, DVM, MS, DABVP (Canine/Feline)
University of Tennessee

In the literature

FROM THE PAGE …

This study surveyed 505 pet owners regarding their perceptions of clinicians based on attire. Respondents reviewed photos of faceless Caucasian men and women in both blue surgical scrubs and business casual attire—with and without an added white coat—and rated their comfort interacting with and perceived competence of clinicians. Higher levels of comfort and competence were associated with surgical scrubs versus business casual clothing. Addition of a white coat increased comfort level.

Because this study was limited to an academic specialty hospital in the midwestern United States, results may differ with other clinics and/or demographics. Faces were not visible, but skin tone was suggestive of a Caucasian demographic; this may also affect individual implicit bias and judgment. In addition, business attire can vary (eg, in style, color, fit, cleanliness, functionality) among individuals, possibly affecting perceptions.

The experience of veterinary patients should also be considered. Whereas a white coat enhanced owner opinion, patients may experience “white coat syndrome,” in which fear, anxiety, and hypertension are associated with the presence of a white coat. Although this concept is extrapolated from human medicine, absence of a white coat may reduce stress in veterinary patients that have had a previously negative experience with a human in a white coat.

Suggested Reading

… TO YOUR PATIENTS
Key pearls to put into practice:

1. Although owners should not base opinions on clothing in place of actions and/or communication skills, first impressions can be lasting, and an owner’s first impression may be based on the clinician’s profile photo on the clinic’s website. It is both acceptable and professional to be photographed in a white coat and scrubs.

2. Clothes worn in the clinic should fit well and be clean, tidy, and functional. An extra set of clothing should be kept in the clinic in case of unexpected staining events. This is especially true for white coats, which can be easily stained and should be disinfected, cleaned, and pressed regularly. Wearing the same white coat between patients can increase the risk for infection.

3. A clinic dress code may be beneficial. Regardless of the attire worn, it should be consistent among all staff members and should be universally decided on based on the culture of the clinic and its clientele. Staff with a similar appearance can indicate a professional and unified team that reflects quality care.
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Osteosarcoma Immunotherapy
for More Days at Home

Osteosarcoma accounts for ≤85% of all primary bone tumors in dogs.1–4 Unfortunately, there have been relatively few advancements to create better outcomes for patients suffering from this cancer. In addition, once the current standard of care (ie, amputation plus chemotherapy for patients with limb tumors) fails, there is little hope of survival. That’s why studying ELIAS Cancer Immunotherapy (ECI) has been exciting for Jeffrey N. Bryan, DVM, MS, PhD, DACVIM (Oncology), professor of oncology at University of Missouri, and member of the ELIAS Animal Health Scientific Advisory Board.5

ECI is the only 2-step immunotherapy in veterinary medicine and has the potential to match or exceed the current standard of care while reducing or eliminating the need for chemotherapy. A form of precision medicine, ECI incorporates both a vaccine pre-treatment made from the patient’s cancer cells and an activated “killer” T-cell immunotherapy. The vaccine introduces mutated proteins to the immune system that serve as markers for which cells to eliminate. This generates antitumor lymphocytes that circulate in the blood. After the 3-vaccine pre-treatment, the antitumor lymphocytes are harvested from the patient’s blood. ELIAS activates and expands them before they are transfused back into the patient (see ECI Treatment Protocol).

Results Backed by Data
Safety and efficacy results support the value of ECI.5,6 Dr. Bryan and his team completed a single-arm, 14-dog pilot study examining ECI osteosarcoma treatment in dogs with no concurrent use of chemotherapy.2 ECI showed better survival outcomes than did other treatment options in previous studies.6,8 Dogs receiving ECI survived an average of 415 days, with 5 surviving past 730 days, which exceeds most median survival times historically reported for patients receiving amputation plus chemotherapy.6 Few other trials show this proportion of osteosarcoma patients living this length of time (Table, next page).5,6,8 Dr. Bryan noted it was rewarding to give patients a better-than-average survival rate and create a greater proportion of long-term survivors.5–8

**ECI Hits the Treatment Target**
Using the patient’s cancer cells to introduce the patient’s particular mutations to the immune system is a well-developed anticancer therapy but, by itself, is rarely successful.5 Coupling autologous cancer vaccination with activated T-cell therapy is unique to ECI. As a result, ECI provides the following potential benefits over chemotherapy and standalone autologous cancer vaccination:

- Eliminates both dividing and dormant cells. Chemotherapy targets rapidly dividing cells to prevent metastatic disease. Osteosarcoma likely includes a

**ECI TREATMENT PROTOCOL**
ECI requires fewer appointments as compared with chemotherapy; this and a close partnership between the primary care veterinarian and specialist make the ECI treatment process easier on the client—and the patient.

**BEFORE ECI**: The primary care veterinarian refers the patient to a veterinary oncologist for aseptic tissue harvesting before amputation. Leaving the limb intact for the oncologist is critical to ensure the collection of viable, plentiful cancer cells. The oncologist performs therapeutic amputation and cell collection before sending tissue to ELIAS for vaccine preparation. ELIAS ships the vaccines back to the oncologist.

**WEEKS 1-3**: The oncologist administers 3 intradermal injections a week apart with the autologous vaccinations prepared from the collected tissue to generate the appropriate immune response. The injection must be intradermal rather than SC to ensure proper presentation to the immune system.

**WEEK 5**: The patient visits a specialty apheresis center for leukapheresis, a procedure in which the immune-stimulated T cells are collected from the patient’s blood. The oncologist sends these T cells to ELIAS, where technicians prepare the T-cell product, then ship it back to the oncologist.

**WEEK 6**: The oncologist performs activated T-cell infusion.

**WEEKS 7-8**: The primary care veterinarian or oncologist performs follow-up interleukin-2 injections. These SC injections are well tolerated and require no specialty training to administer.
large population of metastatic cells not rapidly dividing at the time of treatment. With ECI, cells do not have to be dividing to be eliminated. Instead, they need only to express the mutated abnormal proteins typical of osteosarcoma.

- **Produces durable protection.**Although the underlying immunologic mechanisms involved in ECI are still being investigated, it is possible that the process initiates a population of memory cells that remain in the system.\(^5\) If cancer cells express the same proteins again, which they tend to do, the immune system can continue to suppress the cancer over time.

- **Powerfully activates cell-killing T cells.**When cancers reach a measurable size, they tend to contain a potently immunosuppressive microenvironment that protects them from immune attack. Autologous vaccination educates the immune system that cancer cells are abnormal; however, that re-education alone is not enough to overcome the immunosuppressive environment. Literature has shown that most autologous cancer vaccines have failed to induce strong and durable antitumor immunity.\(^9\) The combination of autologous vaccination and T-cell therapy is critical and associated with the clinical success observed with ECI.

- **Provides more days at home.**The benefits of ECI extend beyond potential treatment success. Chemotherapy often causes severe adverse effects, whereas those associated with ECI are low-grade and transient.\(^6\) In addition, chemotherapy tends to require longer duration of therapy as compared with ECI; therefore, ECI requires fewer trips to the veterinarian and allows for more time in the comfort of home.

**Referring Veterinarians Play an Active Role**

When a primary care veterinarian diagnoses cancer, the next step is to identify the specific cancer type. Aspiration cytology with ALP staining supports the likelihood of bone for tumor origin; this can be performed through radiography to determine tumor location, then through removal of cells with a 22-gauge needle for cytology.

Many veterinarians follow an osteosarcoma diagnosis with immediate leg amputation; ELIAS recommends changing this approach. Immediate amputation eliminates the opportunity to treat with immunotherapy, including ECI. Instead of making amputation the first response, clinicians should consider taking some time to speak with owners about their long-term goals. ECI can provide an alternative to chemotherapy. If owners are interested in ECI, preserving the limb and tumor on the body is vital for ample collection of live cancer cells. With ECI, the specialist performs the amputation, immediately harvesting the tumor and sending the cancer cells to ELIAS for autologous vaccine generation.

Once ECI has been initiated, the general practitioner plays a critical role as the patient’s advocate and care team leader. ECI creates a treatment and communication loop among the primary care veterinarian, oncology specialist, and pet owner and also allows the primary care veterinarian to be highly involved in the treatment process (Table). The specialist completes the more intricate aspects of the procedure while the primary care veterinarian manages most of the patient monitoring without the complexities and risks of handling cytotoxic drugs.

Because the primary care veterinarian can be highly involved in supporting the patient through the immunotherapy process, they remain integral to communicating with the pet owner; thus, clients are more likely to contact the primary care veterinarian with questions. They are also likely to return to the primary care veterinarian for vital follow-up visits and any monitoring required (eg, blood tests, radiography). ELIAS Animal Health has resources to guide primary care veterinarians before, during, and after ECI treatment, and practitioners are always welcome to contact ELIAS directly for support.

**Hope for Dogs & Their Owners**

Hearing their dog has cancer of any kind is scary for pet owners. ECI allows veterinarians to help owners of dogs with osteosarcoma decide which options will give their dog the best chance at long-term survival. Although no veterinarian can definitively predict a treatment outcome, data show that immunotherapy tends to result in the highest chance of long-term remission and lowest rate of recurrence across all cancer types.\(^9\) The ECI trial produced 5 long-term survivors (ie, \(\geq 415\) days).\(^5,6\)

**Conclusion**

The potential benefits of ECI are significant. Patients bounce back from treatments quickly, and after treatment completion, the only follow-ups required are periodic rechecks. In addition, patients can potentially experience longer survival times, as well as fewer appointments and more days at home when receiving ECI as compared with other treatments;\(^6\) which can be a major benefit to pet and owner quality of life.

---

### TABLE

**ECI TRIAL RESULTS: POWERFUL POTENTIAL**

<table>
<thead>
<tr>
<th>Disease-Free Interval</th>
<th>Median Survival Time</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ECI(^*)</strong></td>
<td>213 days(^5)</td>
</tr>
<tr>
<td>COTC 022(^**) (SOC)</td>
<td>180 days(^5)</td>
</tr>
<tr>
<td><strong>ECI(^*)</strong></td>
<td>415 days(^6)</td>
</tr>
<tr>
<td>Amputation alone</td>
<td>134 days(^5)</td>
</tr>
<tr>
<td>COTC 022(^**) (SOC)</td>
<td>267 days(^5)</td>
</tr>
</tbody>
</table>

\(^*\)ELIAS Cancer Immunotherapy  
\(^**\)Comparative Oncology Trials Consortium 022

\(^1\)Although the ECI trial was not randomized, it is unusual that, out of 14 dogs selected without particularly restrictive entrance requirements, 5 survived beyond 2 years. This points to the potential power of ECI for treating canine osteosarcoma.

For references, please visit brief.vet/osteosarcoma

This article was created with the help and expertise of Jeffrey N. Bryan, DVM, MS, PhD, DACVIM (Oncology), professor of oncology at University of Missouri, and member of the ELIAS Animal Health Scientific Advisory Board.\(^7\) Dr. Bryan’s research interests include targeted imaging and therapy and cancer epigenetics and epidemiology. His clinical interests include novel therapy for lymphoma, targeted radiopharmaceutical imaging and therapy, and cancer immunotherapy.
Local Anesthetic Blocks of the Distal Limbs for Dermatologic Procedures

William Oldenhoff, DVM, DACVD
Madison Veterinary Specialists
Monona, Wisconsin

In the literature

FROM THE PAGE …

The distal limb is a common site for dermatologic procedures for both therapeutic and diagnostic purposes. The analgesic protocol should include local anesthesia.

This study reviewed and described the technique of administering regional anesthesia (using either 2% lidocaine or 0.5% bupivacaine) in the distal limbs of dogs and cats. The authors recommend sedation with general anesthesia if necessary (eg, in aggressive patients). The local anesthetic is injected circumferentially around the limb, targeting the major nerves of the distal limb. The manus (ie, distal part of the thoracic limb) is innervated by the radial and median nerves. The pes (ie, distal part of the pelvic limb) is innervated by branches of the common fibular (peroneal) and tibial nerves.

The limb should first be clipped and aseptically prepared. At each injection site, the skin should be tented. On the dorsal aspect of the thoracic limb, the injection is made immediately proximal to the carpus—starting medial to the dewclaw—targeting the superficial branches of the radial nerve and the dorsal branch of the ulnar nerve. On the palmar aspect of the thoracic limb, injection is made on either side of the accessory carpal pad, targeting the median and ulnar nerves. In the pelvic limb, injection is made just distal to the tarsometatarsal joint on both dorsal and plantar aspects, targeting the superficial fibular nerve dorsally, the deep fibular nerve dorsolaterally, and the tibial nerve on the plantar aspect.

Prior to starting the procedure, a maximum dose for the anesthetic should be calculated. For lidocaine, the maximum dose is 6 to 10 mg/kg in dogs and 3 to 5 mg/kg in cats. For bupivacaine, the maximum dose is 2 mg/kg in dogs and 1 to 1.5 mg/kg in cats. A small-gauge needle should be used to inject a bleb of anesthetic after aspiration to ensure the needle is not in a vessel prior to injection. The typical total volume used in dogs weighing <11 lb (5 kg) and in cats is 0.5 mL. In dogs weighting >11 lb (5 kg), typical total volumes used are 1 to 3 mL for both dorsal and palmar blocks. The total dose should be divided between the injection sites; the anesthetic can be diluted with 0.9% saline if additional volume is needed.

… TO YOUR PATIENTS

Key pearls to put into practice:

1. Regional nerve blocks are useful in reducing the amount of sedation needed for a procedure. A ring block of the distal extremity is useful for any painful procedure involving the foot (eg, biopsy or clipping a painful claw). Pet owners may be more comfortable with a procedure when they know that local and regional anesthesia will be used to reduce the amount of sedation needed.

2. The desired time of onset (lidocaine, 10-15 minutes; bupivacaine, 20-30 minutes) and duration of activity (lidocaine, 1-3 hours; bupivacaine, 4-12 hours) should be considered when deciding which local anesthetic agents to use.

3. To avoid toxicity, it is important to calculate the maximum drug dose to ensure the total doses are below the high end of the range.
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INDICATIONS Adequan® Canine is recommended for intramuscular injection for the control of signs associated with non-infectious degenerative and/or traumatic arthritis of canine synovial joints. IMPORTANT SAFETY INFORMATION Adequan® Canine should not be used in dogs who are hypersensitive to PSGAG or who have a known or suspected bleeding disorder. It should be used with caution in dogs with renal or hepatic impairment. Adverse reactions in clinical studies (transient pain at injection site, transient diarrhea, and abnormal bleeding) were mild and self-limiting. In post approval experience, death has been reported in some cases; vomiting, anorexia, depression/lethargy and diarrhea have also been reported. The safe use of PSGAG in breeding, pregnant or lactating dogs has not been evaluated. Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian. For additional safety information, please see Full Prescribing Information at adequancanine.com.

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Dental Disease in Central Bearded Dragons

Thomas H. Boyer, DVM, DABVP (Reptile & Amphibian Practice)
Pet Hospital of Penasquitos
San Diego, California

In the literature

FROM THE PAGE ...

This study represents the first large-scale investigation of risk factors for the prevalence of dental disease in one of the most common captive reptiles—the central bearded dragon (Pogona vitticeps). Data from 20 veterinary clinics in the United Kingdom showed dental abnormalities in half of the examined population of central bearded dragons (n = 304). Only 24.8% of dragons with dental disease exhibited clinical signs, and all of these had advanced dental disease. Central bearded dragons, like chameleons, have acrodont teeth (ie, laterally compressed triangular teeth directly ankylosed to the mandibles and maxilla).1 During development, the pulp of the teeth is lost to a mineralized matrix that fuses teeth to bone.1 In these lizards, teeth are permanent and not replaced throughout life; this is unlike the pleurodont dentition of most other lizards.2 Also unlike other lizards, the gingiva of acrodont lizards does not attach at the base of the teeth; instead, a thin layer of stratified squamous epithelium covers exposed mandibular and maxillary bone, which is predisposed to bacterial colonization.3,4 Acrodonts also lack periodontal ligaments,3 and the authors state that although periodontal disease has been widely described in acrodont reptiles, dental disease is likely a better descriptor.

The authors graded dental disease as normal (grade 0: clinically normal, no dental disease); mild (grade 1: staining of teeth and exposed bone only; grade 2: mild tartar development, gingival erythema); and advanced (grade 3: moderate tartar development, gingival erythema and recession; grade 4: severe tartar buildup, severe gingival erythema and recession, osteomyelitis of jawbones; grade 5: end-stage disease, severe tartar buildup, severe gingival recession, osteomyelitis, pathologic fractures).

The percentage of central bearded dragons with dental disease increased from 11.5% in those <1 year of age to 36.9% in those 1 to 3 years of age and to 86.8% in those >8 years of age.

Continues ➤
The percentage of central bearded dragons with dental disease increased from 11.5% in those <1 year of age to 36.9% in those 1 to 3 years of age and to 86.8% in those >8 years of age. There were significant associations among dental disease, increasing age, being under- or overweight, and concurrent disease. There was also a strong significant association between fruits in the diet and dental disease, with an odds ratio of 2.68; 66% of central bearded dragons with fruits in the diet had dental disease. In contrast, there was no significant association between vegetables in the diet and dental abnormalities or disease. The authors suggested eliminating fruits from the diet, as the high sugar content and acidity of fruits may contribute to dental disease.

**TO YOUR PATIENTS**

Key pearls to put into practice:

1. Thorough oral examination and dental grading are always indicated in central bearded dragons. Dental disease increases with age, but dental cleaning can reduce disease, especially with early detection.

2. Tartar initially supports gram-positive aerobic cocci that shift over time to anaerobic gram-negative bacteria and spirochetes. Fungal infections are less common.

3. In central bearded dragons, diagnosis and treatment of dental disease involve anesthesia with tracheal intubation; cytology; dental radiography; curettage of calculus, gingival sulci, and infected bone with a dental ultrasonic scaler; surgical removal of granulomas; long-term antibiotics—based on aerobic culture and susceptibility testing—that include anaerobic coverage; pain medication; and swabbing or flushing of the labial bones with 0.05% chlorhexidine or oral cleansing gels.

**References**


Let’s face it, 
pilling cats isn’t for everyone.

Fortunately, there’s Profender® – a broad-spectrum, topical dewormer for cats.

Profender® offers a purge deworming of tapeworms, roundworms and hookworms. All in one single, easy-to-apply topical application.†

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- No water chasers
- No messy yellow paste
- No painful injections

† A single treatment is effective and a second treatment should not be necessary. If reinfection with worms occurs, Profender® can be applied after 30 days.

Federal law (U.S.A.) restricts this drug to use by or on the order of a licensed veterinarian. Children should not contact application site for twenty-four (24) hours.
Dear AHS,

I have a client whose 6-year-old Golden Retriever was diagnosed with heartworms late last year. At that time, the dog was given preventive and started on doxycycline. However, the owner was in the midst of a job change and failed to bring the dog back for adulticide administration. While she is now willing to resume treatment, my question is, do I need to re-start the doxycycline—or can I move on to melarsomine? -Dr. M.

THE SHORT ANSWER
If the time span between giving doxycycline and starting melarsomine has been 12 months or less, you can proceed with adulticide treatment.

Interruptions in heartworm treatment are never ideal, as delays can allow heartworm infection to progress. Nevertheless, they are a fact of practice life. At this point, your priority is to restart treatment as soon as possible. The combination of a monthly preventive and 4 weeks of doxycycline treatment should ensure that your patient has—at the very least—not served as a reservoir of heartworm infection to other pets. It’s also vital that the patient stay on heartworm prevention, even if adulticide treatment is delayed.

Here are 3 points to consider when addressing lapses in heartworm treatment:

1. **How long was the lapse?** The AHS heartworm treatment protocol recommends a 30-day interval between the last doxycycline dose and initiation of melarsomine therapy. If no more than 12 months have elapsed since the doxycycline therapy, you can immediately give the first dose of melarsomine, with the second and third doses given 30 and 31 days later. If more than 12 months have gone by, the AHS recommends repeating 4 weeks of doxycycline before giving melarsomine.

2. **What if the patient had already received his or her first melarsomine injection before treatment was paused?** If the elapsed time following the first injection was 6 months or less, it is safe to proceed with the second injection and give the third injection one day later. If the elapsed time is more than 6 months, it will be necessary to repeat the first melarsomine injection, then give the second and third injections on days 30 and 31.

3. **Is the owner resting the pet?** Exercise restriction is essential for dogs with heartworms, because increases in heart rate and blood pressure can contribute to complications from dead and dying worms. Ideally the dog will have been kept calm and quiet since his diagnosis, and the owner will definitely need to keep doing so until 6 to 8 weeks after the last melarsomine injection.

Owner preoccupation, economic hardships such as job loss, owner illness and communication breakdown between owner and veterinarian are common reasons for lapses in heartworm treatment. By getting patients back on the treatment track as soon as possible, you can help ensure that an unintended lapse doesn’t lead to long-term complications for the patient.

American Heartworm Society resources:
- Go to [heartwormtoolkit.com](http://heartwormtoolkit.com) to access the AHS treatment calculator, client handouts and other tools.
- Go to [cagerest.com](http://cagerest.com) for a client handout on helping dogs battle boredom during exercise restriction.

To access the complete set of AHS canine and feline heartworm guidelines, visit [heartwormsociety.org](http://heartwormsociety.org)
Reliability of Refractometers in Measurement of Urine Specific Gravity in Dogs

Anne Barger, DVM, MS, DACVP
University of Illinois

In the literature


FROM THE PAGE …

Urinalysis is a valuable diagnostic tool that consists of a combination of diagnostic tests, including gross evaluation of urine, urine chemistry, sediment examination, and specific gravity. Urine specific gravity (USG) is a critical component of urinalysis and minimum database; it allows for assessment of the ability of renal tubules to dilute or concentrate glomerular filtrate. USG is used in combination with physical examination findings and serum chemistry profile values in the diagnosis of renal disease.

Urine osmolality is considered the gold standard for determining the concentration of the urine. Urine concentration is measured by determining the freezing point of the urine, which decreases with increasing solute in the urine. However, it is impractical to measure urine osmolality in clinical practice, and use of a refractometer to measure USG has been shown to be comparable with measurement of osmolality. All refractometers are not necessarily equal, and there have been studies to evaluate their reliability. One study compared 5 different refractometers (including 1 digital and 2 feline-specific) and found proportional negative bias among them. A second study compared USG measured on canine urine obtained via 4 refractometers with results of measured osmolality; refractometers included 2 optical and 1 digital refractometer, and 3 of 4 were found to be comparable. These studies collectively suggest that comparing results among refractometers could present some clinical challenges.
In this study, the authors evaluated results from 4 different refractometers and evaluated the variability among different users performing USG measurements. Similar to an earlier study, this study showed excellent correlation among refractometers, although one showed constant and proportional biases. Minimal variation of the other refractometers was not clinically relevant. In addition, correlation among users was exceptional. In contrast to other studies, this study found that some refractometers could be used interchangeably and do not appear to have clinically relevant variation and users of variable clinical training could accurately interpret refractometer results with limited training.

... TO YOUR PATIENTS
Key pearls to put into practice:

1. USG is an important component of urinalysis, and certainty of accurate results is crucial.

2. Although this study found excellent agreement between categorization of patient urine concentrations and azotemia, a single USG value should not be used alone; further diagnostics and repeated USG measurements should be performed to confirm categorization of urine concentration and azotemia.

3. Measurement of USG by different users, regardless of experience level, did not appear to result in clinically relevant differences, which is important in clinical practice where various members of staff may be reading USG values.

References

Research Note: Species Identification of Sepsis-Associated Bacteria

Early identification of the causative agent of bacteremia in a septic patient is critical. Standard bacterial culture takes ≥48 hours, and accuracy can be subject to variations in methodology. Matrix-assisted laser desorption/ionization time of flight mass spectrometry (MALDI-TOF MS) is a new method of identifying bacteria by their unique protein fingerprints. Results are usually available in ≈20 minutes. This study evaluated whether MALDI-TOF MS is a reliable tool for use in dogs and cats. Aseptically collected dog and cat blood was inoculated with reference samples of 6 common sepsis-inducing bacteria into a liquid blood-culture medium, which was then analyzed. Species identification obtained through MALDI-TOF MS as compared with classical microbiologic analysis was identical for all 72 samples tested. Investigators concluded that MALDI-TOF MS is reliable for identifying sepsis-inducing bacteria in dogs and cats.

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INDICATION
Galliprant is an NSAID that controls pain and inflammation associated with osteoarthritis in dogs.

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


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See page 60 for product information summary.
GALLIPRANT® (grapiprant tablets)

For oral use in dogs only

20 mg, 60 mg and 100 mg flavored tablets

A prostaglandin E₂ (PGE₂) EP4 receptor antagonist; a non-cyclooxygenase inhibiting, non-steroidal anti-inflammatory drug

Caution:

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

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

Indication:

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

Dosage and Administration:

Always provide “Information for Dog Owners” Sheet with prescription.

Use the lowest effective dose for the shortest duration consistent with individual response.

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

Only the 20 mg and 60 mg tablets of GALLIPRANT are scored. The dosage should be calculated in half tablet increments.

Dogs less than 8 lbs. (3.6 kgs) cannot be accurately dosed.

The 100 mg tablet is not scored and should not be broken in half.

See product insert for complete dosing and administration information.

Contraindications:

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

Warnings:

Not for use in humans. Keep this and all medications out of reach of children and pets. Consult a physician in case of accidental ingestion by humans.

For use in dogs only. Store GALLIPRANT out of reach of dogs and other pets in a secured location in order to prevent accidental ingestion or overdose.

Precautions:

The safe use of GALLIPRANT has not been evaluated in dogs younger than 9 months of age and less than 8 lbs (3.6 kgs) dogs used for breeding, or in pregnant or lactating dogs.

Adverse reactions in dogs receiving GALLIPRANT may include vomiting, diarrhea, decreased appetite, mucoid, watery or bloody stools, and decreases in serum albumin and total protein.

If GALLIPRANT is used long term appropriate monitoring is recommended.

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

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

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

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

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

Adverse Reactions:

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

Table 1. Adverse reactions reported in the field study.

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

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

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

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

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

Information for Dog Owners:

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

Effectiveness:

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

Storage Conditions:

Store at or below 86° F (30° C)

How Supplied:

20 mg, 60 mg and 100 mg flavored tablets in 7, 30 and 90 count bottles

NADA 141-455, Approved by FDA

Manufactured for:

Elanco US Inc.
Greenfield, IN 46140

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November 2018
NSAIDs, Cats, & Anesthesia: Are the Kidneys at Risk?

Berit Fischer, DVM, DACVAA, CCRP
Crown Veterinary Specialists & Associates
Lebanon, New Jersey

In the literature

FROM THE PAGE …

Although NSAIDs can alleviate postoperative pain in healthy cats, potential adverse effects on kidney perfusion often discourage use of these drugs in analgesic protocols.

Most clinically available biochemical tests lack the sensitivity to detect early kidney damage, making it difficult to identify direct cause-and-effect relationships. In research settings, measurement of glomerular filtration rate (GFR) is an effective but time-consuming method to detect acute kidney injury (AKI). N-acetyl-β-D-glucosaminidase (NAG) is a novel, highly specific urine biomarker for renal damage that is predictive of AKI in humans and has been shown to rapidly increase in cats and dogs receiving nephrotoxic drugs.

In this clinical trial, healthy cats were administered carprofen (n = 8), meloxicam (n = 8), or saline (n = 8) SC at the time of preanesthetic medication prior to routine dental prophylaxis. GFR was measured in all 3 groups, and urinary NAG activity was measured in the meloxicam and saline groups 4 hours before and 24 hours after the dental prophylaxis. The goal was to determine whether NSAIDs produced changes in GFR and NAG indicative of AKI. Results demonstrated no significant differences in GFR among the 3 groups or in NAG between the meloxicam and saline groups at either time point. The authors concluded that preanesthetic administration of carprofen or meloxicam did not result in appreciable renal dysfunction in healthy, normotensive cats during the trial period.

It is important to note that NSAID-associated AKI is rarely caused by direct nephrotoxic effects. Rather, it is related to the kidneys’ inability to increase renal perfusion via prostaglandin-mediated vasodilation in times of hemodynamic instability (eg, hypotension). Because no cats in the trial had mean arterial blood pressure below that expected to stimulate prostaglandin release, NSAID-related renal damage was not anticipated.

… TO YOUR PATIENTS
Key pearls to put into practice:

1. Based on this trial, preanesthetic administration of carprofen to healthy, normotensive cats is not associated with changes in GFR that might indicate the presence of renal tubular damage. Preanesthetic administration of meloxicam to healthy, normotensive cats is also not associated with changes in GFR or NAG that might indicate the presence of renal tubular damage.

2. Hypotension is a common and not always predictable complication of anesthesia. The mechanism of NSAID-associated AKI suggests that administration before anesthesia in hypotensive patients may leave the kidney vulnerable.

3. Until further studies elucidate risk in anesthetized, hemodynamically compromised patients, cautious use of preanesthetic administration of NSAIDs in cats is recommended.

References
NEARLY

40%

OF ALL CATS

show clinical signs of osteoarthritis\(^1\)

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Prevalence of Problematic Behaviors in Dogs

John J. Ciribassi, DVM, DACVB
Chicagoland Veterinary Behavior Consultants
Schereville, Indiana

In the literature

FROM THE PAGE …

Behavior problems are a leading reason companion animals (particularly dogs) are relinquished to shelters.1 It can be helpful to ask pet owners specific behavior-related questions during visits to the clinic so veterinary staff can better recognize behavior problems and increase the likelihood that the behavior can be managed.

In this study, owners (representing 401 dogs) visiting a university veterinary hospital in southwest Iran for wellness care were surveyed. Thirteen problematic behaviors were identified, and owners reported ≥1 behavior problem in 86% of dogs; this is similar to the prevalence seen in a separate study performed in the United States.2

Problems identified in this study included excessive activity, fearfulness, destructiveness, roaming, house soiling, excessive barking, coprophagy, withdrawal, mounting/humping, and aggression toward unfamiliar humans, familiar humans, owners, and other dogs. Fearful behavior was more common in small, adult, and female dogs. Aggressive behaviors were more likely in adult dogs and outdoor dogs, whereas indoor dogs showed more fear, withdrawal, and mounting behaviors.

… TO YOUR PATIENTS
Key pearls to put into practice:

1. Owners should be provided with a brief questionnaire that asks about recognized behavior issues in their pet and whether they would like assistance with the problem (see Suggested Reading).3

2. Owner concerns should be addressed during routine consultation. Consult time can be increased if a behavior concern is known in advance. For concerns brought up spontaneously during the visit, a brief discussion of the problem can be held; significant concerns may warrant another visit so the issue can be more fully addressed.

3. Staff should be trained to handle screening and initial discussions with owners and to offer advice regarding basic behavior problems (eg, house soiling, destructive behavior). A full behavior consultation can be scheduled for more in-depth issues (eg, fears, phobias, aggression), or patients can be referred to a qualified veterinary behaviorist.

4. Critical behavior topics (eg, house training, puppy biting, proper play, destructive behavior), puppy class recommendations for dogs 8 to 14 weeks of age, and grooming techniques should be addressed at puppy visits.

References

Suggested Reading
Owner (Mis)Perceptions of CPR

Janine M. Calabro, DVM, DACVECC
Friendship Hospital for Animals
Washington, D.C.

In the literature

FROM THE PAGE …

Although pet owners at the clinic may be asked whether they want cardiopulmonary resuscitation (CPR) performed if their pet goes into cardiac arrest, public perception of CPR survival rates may be inaccurate. This study used a questionnaire to evaluate owner perceptions of CPR; questions included owner demographics, CPR knowledge, reasons for choosing versus declining CPR, and estimated CPR success rates and costs, as well as whether owners work in healthcare and whether owners watch medical television shows. Pet age and species were also included.

Of the 296 surveys analyzed, almost all owners (92%) provided an appropriate basic definition of CPR. Most respondents (76%) had previously taken a human CPR training course, 11% possessed knowledge of how to perform CPR on a dog or a cat, and 67% elected to have CPR performed on their pet at the current visit if necessary. Owners overestimated the likelihood of survival to discharge from the hospital as compared with reports in current literature, and those that elected CPR estimated lower costs associated with resuscitation as compared with owners that declined CPR. Respondents who watched television medical dramas estimated higher rates of survival to hospital discharge. Most respondents (76%) wanted the clinician to make the CPR decision in the event of an arrest, and 82% also wanted to discuss CPR status at the veterinary clinic visit.

This study identified inaccurate perceptions and knowledge gaps regarding CPR among pet owners. Considering the vast majority of respondents expressed interest in discussing CPR status with their clinician, clinicians can help by educating owners, thus enabling them to make better-informed decisions.

… TO YOUR PATIENTS

Key pearls to put into practice:

1. Owners may have inaccurate perceptions about survival rates following CPR.
2. It is important to educate owners about CPR, including costs and anticipated outcomes, so they can provide truly informed consent.
3. The Reassessment Campaign on Veterinary Resuscitation (RECOVER) initiative has created evidence-based guidelines for small animal CPR (see Suggested Reading); these guidelines are being updated.

Suggested Reading
Bisphenol A (BPA) is frequently used in the production of food and beverage containers. BPA is thought to be an endocrine disruptor in humans and it has been suggested to play a role in feline hyperthyroidism. Previous studies identified canned food as a risk factor for hyperthyroidism. This study assessed clinicopathologic data from 69 clinically healthy cats ≥7 years of age and compared them with serum BPA concentrations. All samples had measurable BPA levels. There was no association between BPA and thyroid levels. Further research in cats with hyperthyroidism is warranted.

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Reference

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Histologic Subtypes and Clinical Outcomes in Canine B-Cell Lymphoma

Davis Seelig, DVM, PhD, DACVP
University of Minnesota

In the literature

FROM THE PAGE …

Canine B-cell lymphoma consists of multiple histologically and biologically distinct subtypes, but it is often treated as a single disease with doxorubicin-based, multiagent chemotherapy protocols. Although retrospective studies have reported the prognostic importance of subtype,1,2 clinical importance has not been directly studied in standardized prospective clinical trials.

Identification of subtypes traditionally requires lymph node removal, histopathology, immunohistochemistry, and review by a veterinary pathologist trained in hematopathology. However, because of the time, invasiveness, and cost associated with this approach, a diagnosis of canine lymphoma is more routinely made using fine-needle aspiration and cytology. Because cytology can provide both prognostic and subtyping information, it is increasingly combined with flow cytometry, which can provide rapid and clinically relevant diagnostic and prognostic information for many different subtypes of canine lymphoma.

This study sought to examine the influence of subtype on outcome in dogs with B-cell lymphoma treated with a standardized chemotherapeutic protocol (n = 64), as well as the use of flow cytometry to identify histologic subtype. Flow cytometry was able to diagnose 100% of B-cell lymphoma cases but was unable to identify clear phenotyping differences between the different B-cell lymphoma subtypes.

This study also confirmed that nodal B-cell lymphoma in dogs is a clinically heterogenous disease and there are infrequent subtypes (eg, marginal zone lymphoma) with inferior objective response rates and decreased median survival times as compared with diffuse large B-cell lymphoma; these rates were comparable with some forms of T-cell lymphoma.

… TO YOUR PATIENTS
Key pearls to put into practice:

1. Canine lymphoma comprises a broad group of individual diseases, including clinically slow subtypes with prolonged survival times (>600 days) that do not require systemic chemotherapy. Other subtypes are aggressive, with survival times <200 days.

2. A multimodal approach is important for diagnosing canine lymphoma. Flow cytometry can provide significant prognostic information that may help guide diagnostic and therapeutic decisions.

References

Suggested Reading
ADDRESSING HANDLING AGGRESSION IN PANDEMIC PUPPIES

By Dr. Sally J. Foote, DVM, CABC-IAABC

The pandemic shutdown and stay-at-home orders led to a dramatic increase in pet adoptions as families were able to devote more time to their puppies. However, these circumstances created a unique set of behavioral problems in young dogs.

Veterinarians have reported that handling aggression is a common behavioral problem in general practice. Many of these “pandemic puppies” are resistant to nail trims, ear cleaning and positioning. Puppies have lacked petting, grooming and happy visits resulting in increased squirming, nipping, and struggling during exams. These puppies become dogs who bite when held for nail trims or positioning for treatment.

How handling aggression develops

Aggression is defined as any threat or harmful behavior directed toward a perceived threat. Aggression begins at stare and escalates up to bite. The snapping, head flipping dog is aggression at touch during handling.

Handling aggression often develops when a dog struggles against being held, and the handling is continued. Hanging on tightly to a resistant puppy receiving a vaccine may escalate into anxiousness that turns into biting to force the release.

Even if the puppy is not let go, they have still learned to aggress against the hold. Impulsive behaviors such as grabbing at hands, and jumping up increases agitation and can lead to aggression. The adrenaline rush from activity contributes to the quick switch to aggression.

Many “pandemic puppies” have missed out on pets from strangers, happy visits to the vet clinic and puppy classes. In curbside care, veterinarians have missed the opportunity to teach the puppy to accept handling. The owners are left to working on this at home and may continue to struggle. This escalates the handling aggression resulting in a dog who attempts to bite when picked up or held for an exam.

In curbside care, veterinarians have missed the opportunity to teach the puppy to accept handling. The owners are left to working on this at home and may continue to struggle.

Controlling handling aggression during exams

Handling aggression can develop rapidly. A four-month-old puppy who struggles during a nail trim, turns into the six-month-old dog who bites during paw handling. The following is a guide to help control the aggression and create a less stressful care plan immediately.

1. Assess – Determine what is triggering them and remove or hide that trigger. Get off the exam table and go to a quieter area.

2. Calming products – Add in a pheromone spray, fast-acting medication, or supplement.

3. Alter technique – Change your approach and handling technique. Try approaching from the side instead of front, and avoid handling the paw.

4. Use Rewards – Reward throughout the procedure using a target item to create focus. Food, verbal praise, a toy, or body massage are all rewards. Use what motivates this animal.

5. Make a plan – Record the handling plan in the record and give the client a copy to work on at home.

6. Consider Alternatives – If the above does not diminish struggle reduce aggression, pre-exam calming medication may be beneficial along with a puppy consultant to work with the client.

“Pandemic puppies” have missed many early milestones. Helping these dogs learn to accept handling is important for their health and your safety. Be sure all your staff is consistent in using these safe and effective handling techniques.


Aggression in Pandemic Puppies

Addressing Handling Aggression

Aggression is defined as any threat or harmful behavior directed toward a perceived threat. Aggression begins when a dog struggles against being handled, squirming, nipping, and struggling during exams. These puppies become anxious when a dog struggles against being handled, and the handling is continued. Handling aggression often develops as a result of missed early milestones in a young puppy’s life. Helping these dogs learn to accept handling is important for their health and well-being. "Pandemic puppies" have missed the opportunity to work on this at home and may continue to struggle. This escalates into anxiousness that turns to aggression.

Veterinarians have reported that handling aggression is a common behavioral problem in young dogs. The pandemic shutdown and stay-at-home activity contributed to the quick switch to working on this at home and may continue to struggle. This escalates into anxiousness that turns to aggression. The pandemic shutdown and stay-at-home activity contributed to the quick switch to working on this at home and may continue to struggle. This escalates into anxiousness that turns to aggression.

Handling aggression results from perceived threat. Aggression begins when a dog struggles against being handled, squirming, nipping, and struggling during exams. These puppies become anxious when a dog struggles against being handled, and the handling is continued. Handling aggression often develops as a result of missed early milestones in a young puppy’s life. Helping these dogs learn to accept handling is important for their health and well-being. "Pandemic puppies" have missed the opportunity to work on this at home and may continue to struggle. This escalates into anxiousness that turns to aggression. The pandemic shutdown and stay-at-home activity contributed to the quick switch to working on this at home and may continue to struggle. This escalates into anxiousness that turns to aggression.

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Adverse drug effects can increase morbidity and mortality in dogs, cause emotional stress for pet owners, and increase cost of care. Many (but not all) adverse drug effects can be predicted and therefore prevented. Genetic testing can be used to help identify possible drug effects and determine whether dose adjustments or alternative drug therapies are needed.

Following are the top 5 adverse drug effects that are more likely to occur in specific dog breeds, according to the author.

**1. MDR1 Mutation & Enhanced Susceptibility to CNS Toxicity (Primarily in Herding Breeds)**

P-glycoprotein, encoded by the multidrug sensitivity gene (MDR1 gene, also known as ABCBI gene), functions as a drug transport pump at the blood-brain barrier, preventing potentially toxic compounds from gaining access to the brain. The MDR1 gene mutation (ABCB1-1A) results in production of dysfunctional
P-glycoprotein and affects many herding breed dogs (Table 1) and some nonherding breeds.² Drugs that are P-glycoprotein substrates achieve higher brain concentrations in dogs with the MDR1 mutation (heterozygous or homozygous) than in dogs without the mutation.¹ When P-glycoprotein substrate drugs exert CNS effects, those effects are more pronounced in dogs with the MDR1 mutation unless the dosage is decreased appropriately.¹,³ Thus, dose reductions should be made when possible or an alternative drug should be selected. A nuclear scintigraphy study demonstrated that wild-type MDR1 homozygotes (MDR1 normal/normal) have a fully functional blood-brain barrier with essentially no radioactivity in the brain, whereas MDR1 mutant homozygotes (MDR1 mutant/mutant) have brain radioactivity levels comparable with surrounding tissue, demonstrating a dysfunctional blood-brain barrier with respect to P-glycoprotein substrates (Figure 1).¹ Although many P-glycoprotein substrate drugs (Table 2) exert CNS effects and cause neurologic toxicity in dogs with the MDR1 mutation, some do not and can therefore be administered at usual dosages. MDR1 genotyping should be performed to identify at-risk dogs prior to treatment with P-glycoprotein substrate drugs.⁴

### 2 CYP2B11 Deficiency in Greyhounds & Other Sighthounds

Greyhounds recover more slowly than other dog breeds after receiving certain injectable anesthetic drugs (eg, thiopental, thiamylal, propofol).⁵,⁶ Accumulating evidence suggests this is largely due to decreased liver expression of cytochrome P450 2B11 (CYP2B11; a major drug-metabolizing enzyme) in affected dogs.⁷ CYPB11 metabolizes a range of anesthetic drugs, including propofol, ketamine, midazolam, and medetomidine.⁷,⁹ A mutation in the CYP2B11 gene (CYP2B11-H3) that decreases CYP2B11 expression in vitro was recently identified in greyhounds and certain other sighthound breeds.¹⁰ The mutation has higher prevalence in American Kennel Club-registered greyhounds than in National Greyhound Association-registered greyhounds.¹⁰ This difference may be a consequence of selective breeding for

### Table 1

<table>
<thead>
<tr>
<th>Breed</th>
<th>Approximate Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Collie</td>
<td>70</td>
</tr>
<tr>
<td>Windsprite*</td>
<td>65</td>
</tr>
<tr>
<td>Australian shepherd (all sizes)</td>
<td>50</td>
</tr>
<tr>
<td>McNab</td>
<td>30</td>
</tr>
<tr>
<td>Silken windhound</td>
<td>30</td>
</tr>
<tr>
<td>English shepherd</td>
<td>15</td>
</tr>
<tr>
<td>Shetland sheepdog</td>
<td>15</td>
</tr>
<tr>
<td>German shepherd dog</td>
<td>10</td>
</tr>
<tr>
<td>Herding crossbreed</td>
<td>10</td>
</tr>
<tr>
<td>Crossbreed</td>
<td>5</td>
</tr>
<tr>
<td>Old English sheepdog</td>
<td>5</td>
</tr>
<tr>
<td>Border collie</td>
<td>&lt;5</td>
</tr>
</tbody>
</table>

*Formerly longhaired whippet

![Figure 1](image_url)

**Figure 1** Nuclear scintigraphic images of the brain and surrounding tissue in collies after IV injection of the radiolabeled P-glycoprotein substrate sestamibi (99mTc-sestamibi). P-glycoprotein restricts 99mTc-sestamibi entry into brain tissue of the MDR1 wild-type dog (A), whereas lack of P-glycoprotein allows 99mTc-sestamibi to enter brain tissue of the MDR1 mutant/mutant dog (B).
differently purposes (ie, conformation vs racing speed). \textit{CYP2B11-H3} was also identified in \textgreater 50\% of the sighthound breeds that were evaluated, as well as in some nonsighthound breeds at a lower prevalence (\textit{Table 3}, next page).\textsuperscript{10} Although in vivo validation studies are still needed, \textit{CYP2B11} genotyping might aid in identification of individual dogs likely to demonstrate prolonged effects when receiving drugs that require the \textit{CYP2B11} enzyme for efficient elimination.

\begin{table}[h]
\centering
\caption{DRUGS & THEIR POTENTIAL ADVERSE EFFECTS IN DOGS WITH THE \textit{MDR1} MUTATION\textsuperscript{1,3,12,13}}
\begin{tabular}{|l|l|}
\hline
\textbf{Drug Category} & \textbf{Specific Agent} \\
\hline
\textbf{Neurologic toxicity} & \\
Analgesic & Butorphanol \\
Sedative & Acepromazine \\
Antiparasitic (macrocyclic lactones)\textsuperscript{*} & Doramectin \\
& Eprinomectin \\
& Ivermectin \\
& Milbemycin \\
& Moxidectin \\
& Selamectin \\
Antiparasitic (octadepsipeptide) & Emodipside \\
GI (antidiarrheal) & Loperamide \\
GI (antiemetic) & Ondansetron \\
\textbf{Other toxicities (eg, myelosuppression, GI)} & \\
Chemotherapeutic (antibiotic/antineoplastic agents) & Doxorubicin \\
& Actinomycin D \\
Chemotherapeutic (vinca alkaloids) & Vincristine \\
& Vinblastine \\
& Vinorelbine \\
Chemotherapeutic (taxanes) & Paclitaxel \\
& Docetaxel \\
Immunosuppressant & Cyclosporine \\
\hline
\textsuperscript{*}Should only be administered at label doses; label doses for heartworm prevention undergo safety studies in dogs with the \textit{MDR1} mutation as required by the FDA.
\end{tabular}
\end{table}

\textbf{MDR1 Mutation & Enhanced Susceptibility to Drugs Eliminated via Biliary Excretion (Chemotherapeutics & Other Drugs)}

Adverse drug effects caused by the \textit{MDR1} gene mutation are not limited to neurologic toxicity. Because P-glycoprotein actively transports substrate drugs into the bile, dogs with the \textit{MDR1} mutation have decreased biliary clearance of those drugs normally eliminated via biliary excretion.
TABLE 3

DOG BREEDS KNOWN TO HARBOR THE CYP2B11-H3 MUTATION

<table>
<thead>
<tr>
<th>Breed</th>
<th>CYP2B11-H3 Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sighthounds</strong></td>
<td></td>
</tr>
<tr>
<td>Greyhound (American Kennel Club-registered)</td>
<td>59</td>
</tr>
<tr>
<td>Rhodesian ridgeback</td>
<td>28</td>
</tr>
<tr>
<td>Borzoi</td>
<td>26</td>
</tr>
<tr>
<td>Greyhound (National Greyhound Association-registered)</td>
<td>17</td>
</tr>
<tr>
<td>Italian greyhound</td>
<td>11</td>
</tr>
<tr>
<td>Whippet</td>
<td>11</td>
</tr>
<tr>
<td>Scottish deerhound</td>
<td>11</td>
</tr>
<tr>
<td>Silken windhound</td>
<td>7</td>
</tr>
<tr>
<td>Spanish sighthound</td>
<td>6</td>
</tr>
<tr>
<td>Windsprite*</td>
<td>5</td>
</tr>
<tr>
<td>Ibizan hound</td>
<td>3</td>
</tr>
<tr>
<td><strong>Other breeds</strong></td>
<td></td>
</tr>
<tr>
<td>Golden retriever</td>
<td>12</td>
</tr>
<tr>
<td>Border collie</td>
<td>8</td>
</tr>
<tr>
<td>Labrador retriever</td>
<td>6</td>
</tr>
<tr>
<td>Crossbreed</td>
<td>2</td>
</tr>
</tbody>
</table>

*Formerly longhaired whippet

(CYB5R3 = cytochrome b5 reductase
EACA = epsilon aminocaproic acid

Delayed Postoperative Bleeding in Greyhounds & Other Sighthounds

Significant and occasionally life-threatening postoperative bleeding that starts 24 to 48 hours following surgery has been identified as a significant health concern in greyhounds. Clinical studies suggest the incidence of delayed bleeding can range from 26% following routine gonadectomy to ≤67% following limb amputation for osteosarcoma. Current evidence indicates reduced α2-antiplasmin activity in the plasma of affected dogs, suggesting that bleeding may be secondary to enhanced fibrinolysis of newly formed clots. Both retrospective and placebo-controlled prospective studies have established the effectiveness of treatment with epsilon aminocaproic acid (EACA; Table 4), an antifibrinolytic drug, for preventing delayed bleeding via increased clot strength. Anecdotal evidence suggests Scottish deerhounds are also susceptible to delayed postoperative bleeding and may benefit from preventive antifibrinolytic treatment (EACA or tranexamic acid). A breed-based predisposition to this condition has not yet been reported, but it
is likely caused by a mutation in a gene that regulates fibrinolysis. Although current recommendations are to treat all affected breed dogs, genetic testing for the putative mutation could be used to identify individual dogs that would benefit from prophylactic antifibrinolytic treatment. Identifying dogs of affected breeds that do not require treatment (ie, those that lack the mutation) could also minimize the potential risk for adverse effects of antifibrinolytic drugs (eg, thromboembolism).

Sulfonamide Hypersensitivity in Doberman Pinschers

Hypersensitivity to sulfonamides can manifest as fever, keratoconjunctivitis sicca, hepatotoxicity, skin eruptions, blood dyscrasias, and/or arthropathy and may lead to a mortality rate of 21% in Doberman pinschers. Doberman pinschers have been reported to be particularly predisposed to sulfonamide hypersensitivity, but this is not limited to this breed. A recent study identified an association between a mutation in the cytochrome \( b_5 \) reductase (\( \text{CYB5R3} \)) gene and sulfonamide hypersensitivity. This mutation was determined to be overrepresented in Doberman pinschers and in dogs of other breeds that experienced sulfonamide hypersensitivity reactions. Although \( \text{CYB5R3} \) encodes a drug-metabolizing enzyme, this enzyme does not appear to be directly involved in the metabolism of sulfonamides. Instead, it is likely to be linked to a polymorphism that is directly involved in sulfonamide clearance. When possible, sulfonamides should be avoided in Doberman pinschers.

Conclusion

The physical characteristics of certain dog breeds can provide clues for breed-specific susceptibility to certain adverse drug reactions. Genotyping for specific variants can be used to inform appropriate drug selection and/or dosage modifications. Preventive treatment with EACA or tranexamic acid should be considered in greyhounds and Scottish deerhounds undergoing major surgery after assessment of the risks and benefits to individual dogs.

**TABLE 4**

EACA DOSE RATES CURRENTLY USED FOR THE PREVENTION OF DELAYED POSTOPERATIVE BLEEDING IN GREYHOUNDS & SCOTTISH DEERHOUNDS

<table>
<thead>
<tr>
<th>Dog Weight</th>
<th>EACA Dose*</th>
</tr>
</thead>
<tbody>
<tr>
<td>55-79 lb (25-35 kg)</td>
<td>500 mg (1 tablet)</td>
</tr>
<tr>
<td>80-104 lb (36-47 kg)</td>
<td>750 mg (1.5 tablets)</td>
</tr>
<tr>
<td>&gt;105 lb (&gt;47 kg)</td>
<td>1,000 mg (2 tablets)</td>
</tr>
</tbody>
</table>

*EACA tablets are administered PO every 8 hours for 5 days starting on the day of surgery.
References


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GI signs (eg, vomiting, diarrhea, inappetence) are common presenting complaints in veterinary patients.1 When these signs become chronic (lasting >14 days), they can impact both patient and pet owner quality of life. Obtaining a definitive diagnosis for the cause of chronic GI signs can be difficult, expensive, and sometimes invasive.

**Case Presentation**

Luna, a 5-year-old spayed Labrador retriever crossbreed, is presented for chronic, intermittent diarrhea that has been nonresponsive to medical management. She is up to date on vaccinations and flea/tick and heartworm prevention. During the initial evaluation, the owner notes that Luna vomits bile 2 to 3 times per month. These episodes do not seem to be associated with a particular time of day or event. The owner notes that her bowel movements have been soft over the past few weeks, progressing to liquid stool. A fecal flotation is performed and is negative for ova and parasites. The owner elects to try a short course of a probiotic and bland diet.

At the recheck appointment 1 month later, her owner reports that her stool consistency has improved but has not returned to normal. She is eating well and has resumed her normal adult maintenance diet. She has an appropriate BCS of 4 out of 9 but has lost 5 lb since her annual wellness examination 3 months prior. The physical examination is otherwise unremarkable.

Based on her chronic GI signs, a diagnostic investigation is recommended. Fecal flotation, diarrhea PCR panel, and Giardia spp antigen results are negative. CBC, serum chemistry, urinalysis, and thyroxine (T4) levels are within normal limits. Abdominal radiography does not suggest structural disease or GI obstruction.

**New Diagnostic Test for Dogs with Chronic Gastrointestinal Signs**

Because of the potential adverse effects of immunosuppressants and the invasiveness and expense of obtaining biopsies, a novel diagnostic test for CE/IBD can aid in the investigation of chronic GI signs and benefit both patients and pet owners.

Chronic enteropathy (CE) describes GI conditions causing clinical signs lasting >14 days.2 These signs, including vomiting, diarrhea, inappetence, borborygmi, flatulence, nausea, abdominal pain, and weight loss, result from uncontrolled intestinal inflammation,3 which creates compromise in the mucosal barrier and loss of immunologic tolerance to antigens (ie, food, bacteria) in the GI tract. Antibodies to these antigens are formed, perpetuating inflammation.

CE can be subclassified based on response to treatment as food-responsive enteropathy (FRE), antibiotic-responsive enteropathy (ARE), immunosuppressant-responsive enteropathy (IRE), or non-responsive enteropathy (NRE).3 In >50% of CE cases, dogs have FRE, which can be successfully treated with a novel protein or hydrolyzed diet.3

Although the terms are used interchangeably, CE and inflammatory bowel disease (IBD) are not the same.2,3 CE is used in the absence of histopathology, whereas inflammation must be demonstrated on histopathology to make a diagnosis of IBD.2,3 Immunosuppressant medications are required to treat true IBD.

Because of the potential adverse effects of immunosuppressants and the invasiveness and expense of obtaining biopsies, a novel diagnostic test for CE/IBD can aid in the investigation of chronic GI signs and benefit both patients and pet owners.
What Comes Next?
The owner is offered a choice to pursue a treatment trial for CE, start a hypoallergenic diet trial, or continue the diagnostic investigation, which would include abdominal ultrasonography, resting cortisol, Precision PSL, and Texas A&M GI panel. This approach is typically preferred for any patient with chronic GI signs that is clinically unstable, may have severe clinical signs, and/or may have hypoalbuminemia.

The owner is interested in pursuing further diagnostics in the hopes of obtaining a more definitive diagnosis. The owner is advised that a definitive diagnosis of IBD is based on histopathology obtained via endoscopy (partial-thickness biopsy) or exploratory laparotomy (full-thickness biopsy). Obtaining biopsies allows diffuse neoplasia such as lymphoma to be ruled out; however, biopsies are invasive and expensive and carry anesthesia-associated risks. In addition, there are often minimal changes to the treatment plan when results are received, as histopathology cannot differentiate FFE from ARE and IRE and does not always correlate with severity of clinical signs.

As an alternative next step, the owner is offered a novel serum-based diagnostic test from Antech Diagnostics.

A New Diagnostic Option
Antech’s CE/IBD assay is a rapid and affordable blood test that evaluates 3 serologic biomarkers to help distinguish CE/IBD from other causes of chronic GI signs, guide therapy, and monitor response to treatment. The test has high sensitivity (86%) and specificity (94%) for CE and IBD. Owners should be aware that their pet may still need additional diagnostics with this test and that the gold-standard diagnostic for IBD remains histopathology.

The assay is an ELISA test for:
- **Anti-calprotectin IgA (ACNA):** An additional marker of intestinal inflammation.
- **Antigliadin IgA (AGA):** An antibody to gliadins, a component of gluten. In some types of CE, gliadins can cross the intestinal epithelial barrier due to increased permeability, resulting in AGA production. Presence of AGA indicates possible food sensitivity.

Assay results are either “consistent with CE/IBD” or “not consistent with CE/IBD,” based on biomarker levels. If results are not consistent with CE/IBD, additional diagnostics should be pursued to determine the cause of chronic GI signs. If results are consistent with CE/IBD and the patient is stable, treatment for presumptive CE/IBD can be pursued. However, if the patient is not stable, further diagnostics should be pursued while continuing supportive care.

In addition to the combined results, biomarker levels can help direct treatment. Each biomarker has an interpretive range of values that can determine if the level is low, intermediate, or high. For instance, a gliadin-free diet should be considered in cases of elevated AGA, even if results are not consistent with CE/IBD. If AGA is low, a dietary trial with any novel protein or hydrolyzed diet can be pursued. Elevated ACA suggests prebiotics and probiotics may be useful, as this is a marker of bacterial proliferation.

This test can be used in patients with intermittent or persistent GI signs lasting >14 days, patients with acute GI signs and documented weight loss (suggesting chronically), and monitoring of patients undergoing treatment using serial testing.

Case Results
Assay results are consistent with CE/IBD. ACA is 52.6 and considered high (40 EU/mL), ACNA is 8.9 and considered intermediate (6-15 EU/mL), and AGA is 90.8 and considered high (>60 EU/mL). The client agrees to a dietary trial with a gliadin-free novel protein diet. Because ACA is also elevated, pre- and probiotic therapy are also instituted.

Patients should be retested 2 to 4 weeks after starting initial treatment to evaluate therapeutic response. A decrease in ACA and ACNA values is indicative of reduced intestinal inflammation, and decreased ACA levels are indicative of reduced bacterial proliferation. In cases of elevated AGA, improvement should be expected after starting a gliadin-free diet if clinical signs are due, at least in part, to food sensitivity. If there is no improvement in biomarkers with dietary trial alone, further diagnostics and abdominal imaging should be considered if not already performed. Biopsies should be collected prior to starting immunosuppressant medications.

Luna is retested 4 weeks after starting the dietary trial, prebiotics, and probiotics. ACA is 2.4 and considered intermediate (15-40 EU/mL), ACNA is 5.2 and is now low (<6 EU/mL), and AGA is 51.8 and considered intermediate (50-60 EU/mL). Her stool is normal, and she has gained 3 lb. The owner declines further diagnostics and elects to continue the diet trial alone and retest again in 1 month to monitor response to treatment.

Conclusion
The Antech CE/IBD Assay is an affordable, rapid, and noninvasive test that can aid in the diagnosis of CE and IBD in dogs. Use of the assay can help increase client compliance in obtaining a definitive diagnosis and following treatment recommendations and provides an objective way to monitor response to therapy for each patient. It may also reduce the need for the invasive diagnostics required to obtain histopathology samples.

References
Urinary incontinence secondary to urethral sphincter mechanism incompetence (USMI) is a common issue seen in as many as 1 out of 5 spayed dogs.1 Although PROIN® has historically been an invaluable option for such dogs, twice-daily dosing can be inconvenient and problematic for many pet owners.2

PROIN® ER™ extended-release technology results in steady absorption of the drug, allowing for safe and effective concentrations throughout the day.2 A multicenter clinical field trial of 104 dogs with USMI showed that 75 dogs remained well-controlled after receiving PROIN ER™ for 28 days, and 19 dogs showed improvement in signs of incontinence as compared with when receiving PROIN®.2 In another study, 82.2% of dogs readily consumed PROIN ER™ with or without a small meal.3

Because PROIN® worked well for Annie with no noticeable adverse effects, her veterinarian offered to switch her to PROIN ER™. Upon switching, Annie’s incontinence remained resolved. Her owners were much happier with the more convenient, once-daily dosing. Transitioning to PROIN ER™ requires only a simple dosage adjustment. The dosage for PROIN ER™ is 2-4 mg/kg PO every 24 hours as compared with 1-2 mg/kg PO every 8 to 12 hours for PROIN. No washout period is required.2 PROIN ER™ is a convenient option to manage a common problem. At appropriate dosages, its efficacy is high, and potential adverse effects are minimal. Further, PROIN ER™ can treat a broader range of patients than some other urinary incontinence therapeutics can, making it an easier treatment to prescribe in-house and keep in the clinic’s inventory.2,3

References

For full prescribing information, as well as efficacy and safety information, please visit the PRN Pharmacal website: PRNPharmacal.com
Electrocution Emergency in a Puppy

Jennifer Good, DVM, DACVECC
University of Georgia

Clinical History & Signalment
Charlie, a 6-month-old, intact male crossbreed dog, was presented to an emergency clinic for suspected electrocution after chewing on an electric cord. On the day of presentation, Charlie’s owners found him collapsed on the floor next to a connected (ie, plugged in) power strip and a shredded cord. He was conscious but appeared dull and painful around the face. His owners immediately brought him to the veterinary emergency clinic. Prior to this incident Charlie had been a healthy puppy.

Physical Examination
On physical examination, Charlie was quiet but alert and responsive. Temperature was normal, but pulses were rapid and weak; heart rate was 180 bpm, indicating tachycardia. Mucous membranes were pale pink with a capillary refill time of 3 seconds. Charlie was panting and had slightly increased respiratory effort. Ulcerated burns were appreciated at the commissures of the lips and across the dorsum of the tongue. Cardiothoracic auscultation did not reveal any murmurs or arrhythmias, but increased bronchovesicular sounds and soft crackles were appreciated bilaterally in the caudal pulmonary fields.

Diagnostics
Blood pressure was decreased (85 mm Hg) on Doppler ultrasound. Oxygen saturation was initially 92% but increased to 98% with flow-by oxygen supplementation via mask (4 L/minute). Initial blood work showed mild hyperlactatemia (3.1 mmol/L; reference range, 0-2.5 mmol/L), packed cell volume of 54%, and total solids at 6.8 g/dL. Chest radiography was performed with oxygen supplementation and revealed a moderate to severe caudodorsal interstitial to alveolar lung pattern (Figures 1 and 2, next page).
**DIAGNOSIS:**
**NONCARDIOGENIC PULMONARY EDEMA**

**Diagnosis**
The caudodorsal, bilateral, interstitial to alveolar pattern seen on radiographs is most consistent with noncardiogenic pulmonary edema (NCPE). Other differential diagnoses typically include cardiogenic edema or pneumonia. However, because Charlie was 6 months of age with a normal heart size and no murmurs or arrhythmias auscultated, cardiogenic edema was less likely. Expected pulmonary changes to the lungs are more diffuse with fungal or viral pneumonia or more discrete with bacterial pneumonia. NCPE was most likely in this patient because of the caudodorsal, bilaterally symmetric pattern and history of presumptive electrocution.

**Treatment & Management**
Charlie was placed in an oxygen cage with 40% fraction of inspired oxygen, and a fluid bolus (lactated Ringer’s solution, 10 mL/kg IV) was administered over 20 minutes. Repeated blood pressure reading postbolus was 110 mm Hg. A single dose of a diuretic (furosemide, 1 mg/kg IV), a bronchodilator (terbutaline, 0.01 mg/kg SC every 8 hours), and an analgesic medication (methadone, 0.1 mg/kg IV
ARDS = acute respiratory distress syndrome
NCPE = noncardiogenic pulmonary edema

every 6 hours) were administered. Oral burns were gently cleaned with a diluted oral cleansing solution, and sterile lubrication was applied to the lip commissures. Once respiratory rate and effort improved, an isotonic crystalloid (lactated Ringer’s solution, 60 mL/kg/day IV) was administered.

**Prognosis & Outcome**
Thirty-six hours following initial presentation, Charlie’s respiratory rate and effort were normal without oxygen supplementation. Recheck radiographs showed complete resolution of the former alveolar pattern. He was able to lick wet food despite his oral burns, and methadone and terbutaline were discontinued. Charlie was discharged 48 hours following presentation.

Because Charlie received care in the first few hours after the incident, the prognosis was good, as is generally the case in young patients with neurogenic pulmonary edema secondary to electrocution.

**Discussion**
Young patients are more prone to electrocution, as they are more likely to chew on electric cords. Surface burns are often noted where the electric current entered the body. Injuries are secondary to both the direct effect of the current and to transformation of the current to heat in the body. Other findings in cases of electrocution include cardiac arrhythmia, muscle spasms, spinal cord injury, and collapse.

NCPE Secondary to Electrocution
NCPE secondary to electrocution is a neurogenic pulmonary edema, which is defined as acute respiratory distress triggered by a severe event that causes acute injury to the CNS. Neurogenic pulmonary edema is considered a form of acute respiratory distress syndrome (ARDS) and has its own pathophysiology as compared with other forms of acute respiratory distress syndrome. Other possible causes of neurogenic pulmonary edema include spinal cord injury, subarachnoid hemorrhage, traumatic brain injury, prolonged seizures (eg, clusters, status), and meningitis.

**TREATMENT AT A GLANCE**

- Patients presented with a history of electrocution should undergo a thorough oral examination to evaluate potential burns, ulcerations, fistulas, or dental fractures.
- Careful auscultation for any increased respiratory noise, increased effort, or distress is required.
- Thoracic-focused assessment with sonography for trauma (ie, TFAST) examination is recommended to look for the presence of b-lines, cardiac abnormalities, or pleural fluid.
- Fluid resuscitation with careful monitoring for increased respiratory rate and effort that may indicate edema formation is recommended in patients in hypovolemic shock.
- Oxygen supplementation should be provided until respiratory rate and effort return to normal.
- Bronchodilators may be helpful in patients with respiratory distress secondary to neurogenic pulmonary edema and other forms of NCPE, although the evidence is equivocal.
- Pain medications for burns, wounds, and postfasciculation muscle pain are important in patients after electrocution.
- Most cases of neurogenic pulmonary edema resolve in 1 to 3 days.
NCPE can be present in several forms, including ARDS/acute lung injury (ALI), postobstructive pulmonary edema (POPE), re-expansion pulmonary edema (REPE), and neurogenic pulmonary edema. ALI and ARDS are considered the most serious manifestations of NCPE. ARDS is defined as acute-onset (<72 hours) dyspnea with pulmonary edema in the presence of a normal left heart (ie, noncardiogenic in origin), bilateral distribution on radiographs or CT, high-protein fluid in the airways, or known risk factors. ARDS/ALI is considered an increased permeability edema caused by injury to the pulmonary microvascular endothelial barrier and/or to the alveolar epithelium. Inflammation in the pulmonary capillaries can allow high-protein fluid to leak into air spaces.

Postobstructive Pulmonary Edema

POPE (also referred to as negative pressure pulmonary edema) typically occurs after acute upper airway obstruction (type I) or after relief of a chronic partial airway obstruction (type II). Type I is triggered by forceful inspiration against an obstruction or closed glottis. Increased negative pressure can result in an increase in venous return to the right side of the heart. Increased afterload secondary to negative pressure can decrease cardiac output from the left side of the heart. This combination often results in increased hydrostatic pressure, leading to pulmonary edema. Possible causes of type I POPE include but are not limited to choking/foreign body ingestion, strangulation, near drowning, and laryngeal paralysis. Type II is largely due to expiration against a closed airway over time (eg, brachycephalic airway syndrome, chronic stenosis).

Eventually, forced expiration can cause increased pleural and alveolar pressures, resulting in reduced venous return to the right and left sides of the heart. When the obstruction is relieved with surgery, an acute drop in airway pressures typically occurs, leading to a large increase in venous return. The result is increased hydrostatic pressure leading to pulmonary edema.

Re-Expansion Pulmonary Edema

REPE is rare in small animals and usually occurs after chronically collapsed lungs have been re-inflated. The mechanism involves decreased surfactant in collapsed lobes, reperfusion injury, and free radical formation. The most common risk for REPE is recent repair of a chronic diaphragmatic hernia in which the lungs have been compressed over a long period of time.

Pathophysiology

The pathophysiology of neurogenic pulmonary edema involves several mechanisms that link neurologic, cardiac, and pulmonary conditions. Any event that causes an abrupt and extreme elevation in intracranial pressure carries the greatest risk for neurogenic pulmonary edema. A sudden increase in intracranial pressure can result in compression, ischemia, or damage to the neuronal tissues. This increased pressure can lead to a massive sympathetic surge with release of catecholamines and subsequent vasoconstriction and hypertension, resulting in sudden and marked increase in left ventricular afterload and decreased stroke volume that results in buildup of fluid in the pulmonary vasculature. This increased fluid can cause elevated pulmonary capillary hydrostatic pressure that leads to edema. In addition, α-mediated pulmonary venous constriction is possible even in the absence of systemic hypertension and can result in a direct increase of pulmonary capillary pressure. Radiographs typically show a bilateral alveolar pattern primarily in the caudodorsal quadrant.

Electrocution & Electric Burns

Treatment for electrocution should focus on controlling any sequelae to the event. Shock should...
TAKE-HOME MESSAGES

- NCPE can be due to high permeability edema (ie, ARDS/ALI), postobstructive conditions, or re-expansion of chronically compressed lung lobes or can be secondary to acute, severe CNS injury.
- Neurogenic pulmonary edema is secondary to any abrupt and severe CNS event (eg, seizures, strangulation, electrocution).
- Neurogenic pulmonary edema is primarily due to a large sympathetic surge that can result in a massive release of catecholamines, leading to hypertension and subsequent elevated pulmonary capillary pressures.
- Treatment for neurogenic pulmonary edema consists of oxygen supplementation, cautious fluid administration, bronchodilators, and judicious use of diuretics. In general, use of diuretics is of limited value because edema present in all forms of NCPE, including neurogenic pulmonary edema, tends to have a higher protein content. No more than 1 to 2 doses should be given due to the risk for dehydration and limited value of continued administration. Mechanical ventilation may be required in severe cases.
- Electric shocks that penetrate tissue with low resistance (ie, wet skin or mucous membranes) can result in more serious tissue injury.
- Prognosis for neurogenic pulmonary edema depends on the underlying cause (eg, brain tumor with intracranial bleed vs mild electrocution).

Resolution & Supportive Care
A hallmark of NCPE is quick resolution (usually within 48-72 hours, sometimes more quickly). Edema has been reported to resolve in some humans before the patient presents to the emergency room. Treatment should center around providing supportive care for the lungs (eg, oxygen, bronchodilators, initial diuretic therapy) and addressing any underlying issues.

Prognosis
Prognosis depends on several variables. The underlying cause of NCPE is paramount. Young, otherwise healthy patients with neurogenic pulmonary

Electric burns on the surface of mucous membranes can vary from superficial to full-thickness. Oral cavity burns can manifest as ulcerations but may also include dental fractures or oronasal fistulas. The path the electric current takes through the body is determined by the path of least resistance. Dry skin has more resistance, whereas wet skin/hair coat and mucous membranes have very low resistance and thus are typically the preferred path. An electric current can disrupt normal electrophysiologic impulses, leading to cardiac arrhythmias that should be treated as they appear with antiarrhythmics according to their chamber of origin (eg, atria vs ventricles). In addition to NCPE, respiratory distress can occur secondary to swelling of the oropharynx and/or laryngeal tissues or severe spasm of the muscles of respiration. Serum chemistry changes in these patients depend on the amount of tissue damaged by the electric burns; blood work results are usually unremarkable, but ischemia of large portions of tissue can result in hyperkalemia, myoglobinuria, severe lactic acidosis, and hypoalbuminemia.

Resolution & Supportive Care
A hallmark of NCPE is quick resolution (usually within 48-72 hours, sometimes more quickly). Edema has been reported to resolve in some humans before the patient presents to the emergency room. Treatment should center around providing supportive care for the lungs (eg, oxygen, bronchodilators, initial diuretic therapy) and addressing any underlying issues.

Prognosis
Prognosis depends on several variables. The underlying cause of NCPE is paramount. Young, otherwise healthy patients with neurogenic pulmonary
edema secondary to electrocution and no underlying disease generally have a good prognosis, whereas patients with severe ARDS secondary to pneumonia or sepsis of another origin have a far worse prognosis. These patients have ongoing, increased permeability of the pulmonary vasculature secondary to inflammation and are therefore at risk for continued leakage into the alveoli.1,13 In dogs with neurogenic pulmonary edema secondary to electrocution, prognosis also depends on voltage and type of current (ie, alternating vs direct). High voltage exposure is more serious than low voltage exposure. An alternating current can result in more muscular contractions, which prevent the victim from releasing the power source—this is especially true in humans who may grab a power source with their hands and are unable to let go.3,8,15 The degree of damage can depend on resistance of the tissues from the entry to exit points. It is important to remember that current (ie, amperage) depends on the voltage divided by the resistance of the tissue. Dry skin has a higher resistance, and mucous membranes have a low resistance; thus, voltage going through dry skin may have a lower current versus going through a mucous membrane. Therefore, even a lower voltage cord can cause more damage to wet skin or mucous membranes than to dry tissues.3 Patients with full-thickness burns, necrosis of affected tissues, severe arrhythmias, or profound neurogenic pulmonary edema are less likely to survive than those with superficial burns and mild to nonexistent pulmonary signs.3,13

References
Elura™ (capromorelin oral solution)

20 mg/mL
For use in cats only

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

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

INDICATION:
For management of weight loss drug in cats with chronic kidney disease.

DOSAGE AND ADMINISTRATION:
Administer Elura orally at a dose of 2 mg/kg (0.9 mg/lb) or 0.1 mL/kg (0.045 mL/lb) body weight once daily.

CONTRAINDICATIONS:
Elura should not be used in cats that have a hypersensitivity to capromorelin.

WARNINGS:
Not for use in humans. Keep this and all medications out of reach of children and pets. Consult a physician in case of accidental ingestion by humans.

For oral use in cats only.

Do not use in cats with hypersomatotropism (acromegaly). Elura may increase serum glucose for several hours after dosing. Use in cats with current or historical diabetes mellitus has not been evaluated and use may not be appropriate.

PRECAUTIONS:
Use with caution in cats that may have cardiac disease or severe dehydration. Elura causes transient decreases in heart rate and blood pressure up to 4 hours following dose administration. Some cats may exhibit clinical signs of hypotension following administration of Elura. Use with caution in cats with hepatic dysfunction.

Capromorelin is metabolized in the liver in humans and dogs and similar metabolism is expected in the cat. The safe use of Elura has not been evaluated in cats younger than 5 months old. The safe use of Elura has not been evaluated in cats that are pregnant, lactating, or intended for breeding.

ADVERSE REACTIONS:
Safety was evaluated in a 56-day field effectiveness study in 178 client-owned cats (118 administered Elura, 58 administered vehicle control) that received at least one dose. Cats enrolled had ≥5% unintended weight loss and a history of chronic kidney disease (CKD). Cats had a mean age of 15 years and at enrollment 11.4% of the cats were in Stage 1 CKD, 66.5% were in Stage 2, 21.0% were in Stage 3, and 1.1% were in Stage 4. Cats enrolled in the study had a variety of comorbid conditions: dental disease (66.1%), moderate or severe muscle loss (42.4%), heart murmur (28.4%), history of vomiting or overturning gastrointestinal disease (28.4%), hyperthyroidism (13.6%) and hypertension (9.7%).

Table 1: Adverse Reactions in the Field Effectiveness Study

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>ELURA (n=118)</th>
<th>Vehicle Control (n=58)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vomiting</td>
<td>25 (21.2%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Inappetence</td>
<td>22 (18.6%)</td>
<td>7 (12.0%)</td>
</tr>
<tr>
<td>Behavior Change</td>
<td>17 (14.4%)</td>
<td>3 (5.2%)</td>
</tr>
<tr>
<td>Lethargy</td>
<td>16 (13.8%)</td>
<td>6 (10.3%)</td>
</tr>
<tr>
<td>Anemia</td>
<td>11 (9.3%)</td>
<td>11 (19.3%)</td>
</tr>
<tr>
<td>Dehydration</td>
<td>11 (9.3%)</td>
<td>2 (3.4%)</td>
</tr>
<tr>
<td>Stage of CKD Increased</td>
<td>10 (8.5%)</td>
<td>3 (5.2%)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>9 (7.6%)</td>
<td>2 (3.4%)</td>
</tr>
<tr>
<td>Urinary Tract Infection</td>
<td>8 (6.8%)</td>
<td>2 (3.4%)</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>8 (6.8%)</td>
<td>2 (3.4%)</td>
</tr>
<tr>
<td>Upper Respiratory Infection</td>
<td>7 (5.9%)</td>
<td>1 (1.7%)</td>
</tr>
<tr>
<td>Hypercalcemia</td>
<td>7 (5.9%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Facial Skin Lesion</td>
<td>6 (5.1%)</td>
<td>3 (5.2%)</td>
</tr>
<tr>
<td>Hyperkalemia</td>
<td>5 (4.2%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Ataxia</td>
<td>4 (3.4%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>1 (0.8%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Congestive Heart Failure</td>
<td>1 (0.8%)</td>
<td>0 (0.0%)</td>
</tr>
</tbody>
</table>

Note: If an animal experienced the same event more than once, only the first occurrence was tabulated.

* Behavior change included hiding from the owner (8 ELURA, 1 vehicle control); owner reported difficulty administering medication (9 ELURA, 1 vehicle control); and redirected aggression to another household cat (2 ELURA, vehicle control).

† 2 ELURA and 1 vehicle control cat increased by two CKD stages; 8 ELURA and 2 vehicle control cats increased one CKD stage. It could not be determined if the progressive renal disease was the natural course of the pre-existing disease or treatment related.

Hypersalivation was generally associated with dosing and resolved within a few minutes.

Nine cats (8 ELURA and 1 vehicle control) either died or were euthanized during or shortly after the study. Six ELURA cats were euthanized or died from decompensated CKD. One ELURA cat was euthanized after study withdrawal on Day 33 for declining quality of life and recent identification of a new mass. One ELURA cat acutely declined and was euthanized for findings of nodules in both kidneys and diagnosis of sarcoma. The vehicle control cat was euthanized for acute onset of right hindlimb paresis and suspected embolic event. Two additional cats were diagnosed with neoplasia during the study (one ELURA cat with unipsed soft tissue sarcoma and one control cat with mammary adenocarcinoma) but completed the study. In voluntary post-approval reporting for extra-label use of a capromorelin product for dogs, the following adverse events have been reported in cats (listed in decreasing order of reporting frequency): tachycardia, lethargy, hyperventilation, hypotension, behavior change, and vomiting.

To report suspected adverse events, for technical assistance or to obtain a copy of the Safety Data Sheet (SDS), contact Elanco US Inc, 1-888-545-5973.

For additional information about adverse drug experience reporting for reporting animals, contact FDA at 1-888-FDA-VETS or http://www.fda.gov/reportanimalae.

EFFECTIVENESS:
Effectiveness was demonstrated in a multicenter, prospective, masked, randomized, vehicle-controlled field study. The study enrolled 176 client-owned cats with ≥5% unintended weight loss and a history of chronic kidney disease. The cats enrolled included 96 females and 80 males of various breeds, 4.4 – 22.1 years old with a mean age of 15 years and weighing 1.81 – 6.76 kg. CKD stage was determined based on creatinine at screening according to the International Renal Interest Society (IRIS) 2015 guidelines. All stages were enrolled. Cats were administered ELURA at 2 mg/kg or a matched volume of control once daily by mouth for 56 days. The control was the solution without capromorelin (vehicle control). The primary effectiveness variable was the percent change in body weight from Day 0 to Day 55. Effectiveness was evaluated in 112 cats: 71 cats administered ELURA and 41 cats administered vehicle control. There was a statistically significant difference between the percent change in weight for the ELURA group (+5.2%) compared to the vehicle control group (-1.6%) at Day 55 (p<0.0001). Secondary analysis for percent change in weight at Day 15 and Day 27 demonstrated cats in the ELURA group gained weight throughout the study.

STORAGE CONDITIONS:
Store at or below 88°F (30°C)

HOW SUPPLIED:
20 mg/mL flavored oral solution in a 15 mL bottle with an oral dosing syringe.

Approved by FDA under NADA #141-536.

Manufactured for: Elanco US Inc, Greenwood, IN 46140 USA

REV. DATE-10/2020

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PA0028298

July/August 2021

cliniciansbrief.com
Elura helps cats with CKD maintain or gain weight to keep them feline fabulous

It can be hard to watch cats with chronic kidney disease (CKD) waste away. Prescribe Elura at the first sign of weight loss in your feline CKD patients.

INDICATION
For the management of weight loss in cats with chronic kidney disease.

IMPORTANT SAFETY INFORMATION
For oral use in cats only. Do not use in cats that have a hypersensitivity to capromorelin, or in cats with hypersomatotropism (acromegaly). Elura may increase serum glucose for several hours after dosing; use in cats with current or historical diabetes mellitus has not been evaluated and may not be appropriate. Use with caution in cats that may have cardiac disease, severe dehydration, or hepatic dysfunction. Elura has not been evaluated in cats younger than 5 months of age, or in breeding, pregnant or lactating cats. The most common adverse reactions included vomiting, hypersalivation, inappetence, behavior change and lethargy. Please see accompanying brief summary for product safety information.

MORE THAN 8/10 CATS GAINED WEIGHT*1
UNIQUE MOA MIMICS THE NATURALLY OCCURRING HORMONE GHRELIN
SAFE TO USE DAILY AND APPROVED FOR LONG-TERM USE
ORAL SOLUTION WITH LOW DOSING VOLUME

*4/10 cats in the control group maintained or gained weight. A multi-center, placebo-controlled, randomized and masked field study including 176 cats with CKD and at least 5% unintended loss of body weight (as compared to the highest weight in the medical records for the 3 years preceding enrollment). Study period was 56 days (Day 0 – Day 55). Primary endpoint was percent change in weight from Day 0 to Day 55.

CKD, chronic kidney disease.


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See page 87 for product information summary.
1. **CONSULT THE EXPERT PAGE 10**

Nutritional support for patients in the intensive care unit should only be discontinued after the patient is able to consume ________ of their normal resting energy requirement.

A. ≈65%
B. ≈75%
C. ≈85%
D. ≈95%

2. **PROCEDURES PRO PAGE 23**

Which of the following statements regarding pelvic limb amputation is _false_?

A. Complete presurgical orthopedic and neurologic examination is necessary.
B. Increased BCS negatively correlates with quality-of-life score.
C. A midfemoral amputation technique is less likely to result in pressure sores.
D. Amputations typically have a good prognosis.

3. **TOP 5 PAGE 71**

Doberman pinschers are particularly susceptible to which of the following adverse drug effects?

A. CNS toxicity from drugs that are P-glycoprotein substrates
B. Increased drug exposure from drugs eliminated via the biliary system
C. Slower recovery from injectable anesthetics
D. Sulfonamide hypersensitivity

4. **CASE IN POINT PAGE 81**

Noncardiogenic pulmonary edema usually resolves within ___________.

A. 48 to 72 hours
B. 72 to 96 hours
C. 5 to 7 days
D. 1 to 2 weeks

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**Answer Key:**

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

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Boehringer Ingelheim Animal Health continues to put patients first

**NexGard** (afoxolaner)
The chew vets and dogs both choose

**HEARTGARD® Plus**
(ivermectin/pyrantel)
Client-requested, time and again

**FRONTLINE®**
Building on a legacy of patient protection

HEARTGARD® Plus is safe for puppies six weeks or older. NexGard® is safe for puppies at eight weeks, weighing four pounds or more.


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Keep your shelves stocked with triple-action FRONTLINE® Gold brand products, and our newest product, FRONTLINE® Shield for Dogs with FRONTLINE’s fastest speed of kill and added repellency.

**FRONTLINE® Gold for Dogs**

- **Breaks the flea life cycle** by killing the next generation of flea eggs and larvae
- **Kills ticks** including those that may transmit Lyme disease
- **Works for a full month**

**FRONTLINE® Shield for Dogs**

- **Fastest** FRONTLINE product, starts killing fleas in just 5 minutes*
- **Repels** mosquitoes that may transmit heartworm disease and ticks that may transmit Lyme disease
- **Kills** fleas and ticks for a full month

Contact your Boehringer Ingelheim Sales Representative for more information about the #1 name in flea and tick protection.

*Beginning 2 days after treatment
†FRONTLINE brand products. Data on file at Boehringer Ingelheim.

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Assessment was conducted by IDEXX® and leveraged veterinary clinic PIMS transaction level data for 2019. This analysis included data from approximately 7,000 U.S. clinics that had consistent data from 2017 to 2019. To be included, patients needed to have at least one parasiticide transaction in the baseline year (2018). The analysis was limited to loyal patients, where loyalty was defined as having one flea/tick control brand during the full three-year period. The average number of months of NexGard purchased per year was 6.64, compared to 6.69 for BRAVECTO. This analysis overestimates the duration of efficacy for BRAVECTO. For comparison purposes, each BRAVECTO chew was assessed as providing three months of flea & tick protection versus the labeled 12-week coverage for fleas and three species of ticks, and 8-week coverage for Lone Star ticks.

1. Data on file at Boehringer Ingelheim.  2. Data on file at IDEXX Laboratories, Inc. Westbrook, Maine USA.

NexGard® (afoxolaner) is FDA-approved to prevent Lyme infections by killing black-legged ticks.

It’s safe for puppies as young as 8 weeks, weighing as little as 4 pounds.

The savory, beef-flavored chew was designed with compliance in mind:

• NexGard is a leader in average number of months of flea and tick control purchased per patient per year.*2
• More NexGard users purchased a full 12 months of flea and tick protection than users of any other flea and tick chew.*2

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 NexGardClinic.com.

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1. Data on file at Boehringer Ingelheim.  2. Data on file at IDEXX Laboratories, Inc. Westbrook, Maine USA.
FRONTLINE product, starts killing
Learn more at NexGardClinic.com:

- Fastest fleas in just 5 minutes*
- Repels mosquitoes that may transmit heartworm disease
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breaks the flea life cycle with FRONTLINE’s fastest speed of kill and added repellency.

FDA-approved to prevent Lyme infections

#1 name in flea and tick protection.

Information about the product, including those that may be young as 8 weeks, weighing as little as 4 pounds.

FOR YOUR PATIENTS

Contact your Boehringer Ingelheim Sales Representative for more information about the product, including those that may be young as 8 weeks, weighing as little as 4 pounds.

NexGard is a leader in average number of months of flea and tick protection. More NexGard users purchased a full 12 months of protection than users of any other flea and tick chew.*2

• Safe and trusted heartworm disease prevention that's still #1 after 33 years1
• The #1 dog-preferred, real-beef chew that makes compliance enjoyable for pets and pet owners2
• Highly effective control of five species of common intestinal parasites3,4
• Prevention backed by the HEARTGARD Plus Satisfaction Guarantee

Get clinic support at HEARTGARDClinic.com

IMPORTANT SAFETY INFORMATION: HEARTGARD® Plus (ivermectin/pyrantel) is well tolerated. All dogs should be tested for heartworm infection before starting a preventive program. Following the use of HEARTGARD Plus, digestive and neurological side effects have rarely been reported. For more information, please see full prescribing information or visit www.HEARTGARDClinic.com.

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Numerous wildlife species have played a major role in the growth and expansion of parasitic diseases in North America. This article will focus upon three wildlife species and their contribution to flea (opossum), tick (white-tailed deer) and heartworm (coyote) populations.

While the cat flea, *Ctenocephalides felis* is a natural parasite of cats and dogs, a number of other warm-blooded animals in North America are also commonly infested by *C. felis*. The cat flea has been found parasitizing bobcats, coyotes, dairy calves, ferrets, domesticated rabbits, Florida panthers, opossums, red and gray foxes, raccoons, several rodent species, skunks and poultry. Of the native wildlife, the opossum is the most clinically important *C. felis* host.

In San Bernadino, Los Angeles and Orange Counties, 99.8%, 99.1% and 93.8%, respectively of the fleas recovered from opossums were *C. felis*. Similarly in Statesboro, GA, and Manhattan, KS, the most common flea species recovered from opossums was *C. felis*. While the opossum is nocturnal, it is frequently observed by pet owners in their yards. In Tampa, Florida, in 2013, 27 of 37 (73%) home owners with documented flea infestations of their pets and homes reported seeing opossums in their yards. With such a large number of *C. felis* infested opossums living in close proximity to humans and their pets, they are likely causing substantial flea infestation pressure.

Tick infestations and the diseases they transmit are a major concern in North America. Between 2013 and 2019 in a nationwide survey, ≈1.9 million dogs tested antibody positive for *Borrelia burgdorferi*, ≈950,000 tested positive for *Ehrlichia spp.* and ≈1 million tested positive for *Anaplasma spp.* While these antibody tests do not denote the number of dogs with clinical disease, they do indicate just how many dogs are being parasitized by pathogen infected ticks. Over the past several decades changes in climate, host abundance, as well as row crop and forestry practices, have contributed to the increased range and population growth of two important disease carrying tick species *Amblyomma americanum* (Lone Star tick) and *Ixodes scapularis* (black-legged tick or Lyme disease tick).

While wildlife clearly have a role in flea infestations, they are the primary driving force behind tick infestations and tick transmitted diseases. Numerous mammals and birds serve as natural evolutionary hosts for immature and mature tick life stages. In fact, host population density often dictates tick populations and disease transmission rates. One wildlife species and its relation to tick populations...
that has been extensively studied is the white-tailed deer. The white-tailed deer [Figure 1] is the preferred reproductive host for both *Amblyomma americanum* and *Ixodes scapularis*.1,10

During the 18th and 19th centuries the extensive loss of habitat (deforestation and expansion of row crops) and extensive unregulated hunting decimated deer populations.3 By the end of the 19th century only an estimated 300,000 to 500,000 deer remained in North America.12 Concern for the survival of the species ultimately led to restrictions on deer hunting and many states initiated restocking efforts. Combined with increase in natural habitat and by now an almost complete loss of natural predators (wolves, bears and mountain lions) across much of their natural range, deer populations exploded, peaking in 2000 at 38.1 million.23 This remarkable growth in deer populations led directly to population increases of *Amblyomma americanum* and *Ixodes scapularis* and associated tick transmitted diseases of dogs and/or cats, such as Lyme disease (*B. burgdorferi*) and granulocytic ehrlichiosis (*A. phagocytophilum*) for *I. scapularis* and *Cytaxusoonosis (Cytaxusoxen felis), Ehrlichiosis (Ehrlichia ewingii)*, Tularemia (*Francisella tularensis*), and Rocky Mountain Spotted Fever (*Rickettsia rickettsii*) for *A. americanum*.2 As discussed, tick population growth is often directly related to increased white-tailed deer populations and, conversely, populations of *Amblyomma americanum* and *Ixodes scapularis* can dramatically plummet in a few years if deer are excluded from an ecosystem.1

Heartworm disease of dogs and cats caused by *Dirofilaria immitis* is a potentially devastating clinical disease. Even with decades of education on the importance of chemoprophylaxis, a review of 47 million heartworm antigen tests conducted by a commercial diagnostic laboratory between 2013 and 2019 showed that 1.4% (651,000) of the dogs tested positive.9 While veterinarians have correctly focused on the major problem of compliance, they rarely concern themselves with the importance of wildlife reservoirs, particularly the coyote [Figure 3]. A number of surveys from across North America have documented just how commonly coyotes are infected with *D. immitis*. Infections in coyotes range from a low of 7% in Missouri,12 21-41% in Illinois,13 and as high as 51.6% in Georgia.14 Infection rates can vary widely in some states like California, where in some regions infection rates are as low as 0%, while in the coastal foothills prevalence can be as high as 92%.15,16 Given these infection rates, it is clear that coyotes with circulating microfilariae are a major reservoir for *D. immitis.*

Regardless of how many dogs and cats are ever placed on heartworm, flea and tick chemoprophylaxis, these parasites will be ever-present due to their presence in/on native wildlife species and therefore prevention will always be necessary.

References


Photography

Figure 1. Opossum, Boehringer Ingelheim
Figure 2. White-tailed deer. Michael W. Dryden, DVM, PhD, DACVM
Figure 3. Coyote on a golf course. Michael W. Dryden, DVM, PhD, DACVM
HEARTGARD Plus is recommended for dogs 6 weeks of age and older. For dogs over 100 lb use the appropriate combination of these chewables.

ADMINISTRATION: Remove only one chewable at a time from the foil-backed blister card. Return the blister card with the remaining chewables to the box to protect the product from light. Because most dogs find HEARTGARD Plus palatable, the product can be offered to the dog by hand. Alternatively, it may be added intact to a small amount of dog food. The chewable should be administered in a manner that encourages the dog to chew, rather than to swallow without chewing. Chewables may be broken into pieces and fed to dogs that normally swallow treats whole. 

CAVEAT: If the interval between doses exceeds a month (30 days), the efficacy of ivermectin can be reduced. Therefore, for optimal performance, the chewable must be given on or about the same day of the month. If it is suspected that any of the chewables has been lost, recheck all remaining. 

HEARTGARD Plus should be given at monthly intervals during the period of the year when mosquitoes (vectors), potentially carrying infective heartworm larvae, are active. The initial dose must be given within a month (30 days) after the dog’s first exposure to mosquitoes. The final dose must be given within a month (30 days) after the dog’s last exposure to mosquitoes. 

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 for a total of six treatments. There were no clinically-relevant effects related to treatment on physical examination, body weight, food consumption, clinical pathology (hematology, clinical chemistries, or coagulation tests), gross pathology, histopathology or adverse reactions. 

In a well-controlled field study, no adverse reactions were observed from the concomitant use of NexGard with other medications. 

All dogs should be tested for existing heartworm infection before starting treatment with HEARTGARD Plus which is not effective against adult D. immitis. Infected dogs must be treated to remove adult heartworms and microfilariae before initiating a program with HEARTGARD Plus. 

While some microfilariae may be killed by the ivermectin in HEARTGARD Plus chewables, a high hypersensitivity-type reaction, presumably due to dead or dying microfilariae and particularly involving a transient diarrhea, has been observed in clinical trials with ivermectin alone after treatment of some dogs that have circulating microfilariae. 

Keep this and all other drugs out of the reach of children. 

In case of ingestion by humans, clients should be advised to contact a physician immediately. Physicians may contact a Poison Control Center for advice concerning cases of ingestion by humans. 

Data Sheet (SDS), contact Boehringer Ingelheim Animal Health USA Inc. at 1-888-657-8351. 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.

HEARTGARD Plus has been shown to be bioequivalent to HEARTGARD, with respect to the bioavailability of ivermectin. The dose regimens of HEARTGARD Plus and HEARTGARD are the same with regard to ivermectin (6 mcg/kg). Studies with ivermectin indicate that certain dogs of the Collie breed are more sensitive to the effects of ivermectin administered at slightly higher levels (more than 16 times the target level) than other breeds of dogs. At elevated doses, sensitive dogs showed adverse reactions which included mydriasis, paresis, ataxia, tremors, drooling, panting, hyperventilation, mydriasis, stupor, coma and death. HeartGARD demonstrated no signs of toxicity at 10 times the recommended dose (60 mcg/kg) in sensitive Collies. In clinical trials and bioequivalence studies, the safety of HeartGARD products in dogs, including Collies, when used as recommended.

HEARTGARD Plus has shown a wide margin of safety at the recommended dose level in dogs, including pregnant or breeding bitches, and in puppies aged 6 or more weeks. In clinical trials, many commonly used flea collars, dips, shampoos, antihelminthic, antibiotics, vaccines and steroid preparations have been administered with HEARTGARD Plus in heartworm disease prevention program.

In one trial, where some puppies had parvovirus, there was a marginal reduction in efficacy against intestinal nematodes, possibly due to a change in intestinal transit time. 

In case of ingestion of HEARTGARD Plus, vomiting or diarrhea within 24 hours of dosing was rarely observed (1.1% of administered doses). The following adverse reactions have been reported following the use of HEARTGARD: Depression/lethargy, vomiting, anorexia, diarrhea, mydriasis, ataxia, agitation, convulsions and hyperthermia. 

To report suspected adverse drug events, for technical assistance, or to obtain a copy of the Safety Data Sheet (SDS), contact Boehringer Ingelheim Animal Health USA Inc. at 1-888-657-8351. 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.

SAFETY: HEARTGARD Plus has been shown to be bioequivalent to HEARTGARD, with respect to the bioavailability of ivermectin. The dose regimens of HEARTGARD Plus and HEARTGARD are the same with regard to ivermectin (6 mcg/kg). Studies with ivermectin indicate that certain dogs of the Collie breed are more sensitive to the effects of ivermectin administered at slightly higher levels (more than 16 times the target level) than other breeds of dogs. At elevated doses, sensitive dogs showed adverse reactions which included mydriasis, paresis, ataxia, tremors, drooling, panting, hyperventilation, stupor, coma and death. HEARTGARD demonstrated no signs of toxicity at 10 times the recommended dose (60 mcg/kg) in sensitive Collies. In clinical trials and bioequivalence studies, the safety of HeartGARD products in dogs, including Collies, when used as recommended.

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HOW SUPPLIED: HEARTGARD Plus is available in three dosages strengths (see Doseage Section) for dogs of different weights. Each strength comes in convenient cartons of 6s and 12 chewables. 

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