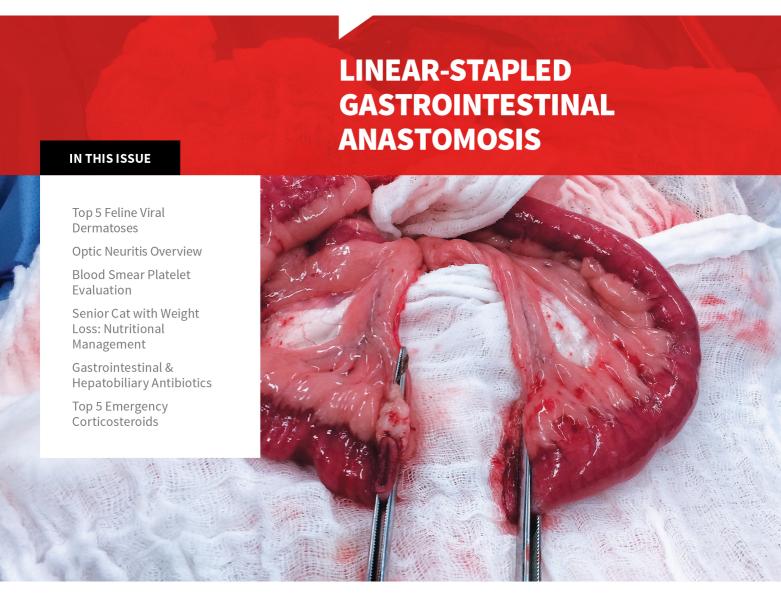
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(florfenicol, terbinafine, mometasone furoate) Otic Solution

Antibacterial, antifungal, and anti-inflammatory For Otic Use in Dogs Only

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

DESCRIPTION:

CLARO® contains 16.6 mg/mL florfenicol, 14.8 mg/mL terbinafine (equivalent to 16.6 mg/mL terbinafine hydrochloride) and 2.2 mg/mL mometasone furoate. Inactive ingredients include purified water, propylene carbonate, propylene glycol, ethyl alcohol, and polyethylene glycol.

INDICATIONS:

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

DOSAGE AND ADMINISTRATION:

Shake before use.

CLARO® should be administered by veterinary personnel.

Administer one dose (1 dropperette) per affected ear. The duration of effect should last 30 days.

- 1. Clean and dry the external ear canal before administering the product.
- $2. \ \ Verify the tympanic membrane is intact prior to administration.$
- $3. \ \ Remove single dose dropperette from the package.$
- $4. \ \ While holding the dropper ette in an upright position, remove the cap from the dropper ette.$
- 5. Turn the cap over and push the other end of the cap onto the tip of the dropperette.
- 6. Twist the cap to break the seal and then remove cap from the dropperette.
- 7. Screw the applicator nozzle onto the dropperette.



8. Insert the tapered tip of the dropperette into the affected external ear canal and squeeze to instill the entire contents (1 mL) into the affected ear.



- 9. Gently massage the base of the ear to allow distribution of the solution.
- Repeat with other ear as prescribed.

 $\label{eq:continuous} \mbox{ Geaning the ear after dosing may affect product effectiveness.} \\$

CONTRAINDICATIONS:

Do not use in dogs with known tympanic membrane perforation (see **PRECAUTIONS**). CLARO® is contraindicated in dogs with known or suspected hypersensitivity to florfenicol, terbinafine hydrochloride, or mometasone furoate.

WARNINGS

<u>Human Warnings</u>: Not for use in humans. Keep this and all drugs out of reach of children. In case of accidental ingestion by humans, contact a physician immediately. In case of accidental skin contact, wash area thoroughly with water. Avoid contact with eyes. Humans with known hypersensitivity to florfenicol, terbinafine hydrochloride, or mometasone furoate should not handle this product.

Do not administer orally.

PRECAUTIONS:

The use of CLARO® in dogs with perforated tympanic membranes has not been evaluated. The integrity of the tympanic membrane should be confirmed before administering the product. Reevaluate the dog if hearing loss or signs of vestibular dysfunction are observed during treatment. Use of topical otic corticosteroids has been associated with adrenocortical suppression and latrogenic hyperadrenocorticism in dogs (see **ANIMAL SAFETY**).

Use with caution in dogs with impaired hepatic function (see ANIMAL SAFETY).

The safe use of CLARO® in dogs used for breeding purposes, during pregnancy, or in lactating bitches has not been evaluated.

ADVERSE REACTIONS:

In a field study conducted in the United States (see **EFFECTIVENESS**), there were no directly attributable adverse reactions in 146 dogs administered CLARO®.

To report suspected adverse drug events and/or obtain a copy of the Safety Data Sheet (SDS) or for technical assistance, contact Baver HealthCare at 1-800-422-9874.

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.

PHARMACOLOGY:

CLARO® Otic Solution is a fixed combination of three active substances: florfenicol (antibacterial), terbinafine (antifungal), and mometasone furoate (steroidal anti-inflammatory). Florfenicol is a bacteriostatic antibiotic which acts by inhibiting protein synthesis. Terbinafine is an antifungal which selectively inhibits the early synthesis of ergosterol. Mometasone furoate is a glucocorticosteroid with anti-inflammatory activity.

MICRORIOLOGY

The compatibility and additive effect of each of the components in CLARO® solution was demonstrated in a component effectiveness and non-interference study. An *in vitro* study of organisms collected from clinical cases of otitis externa in dogs enrolled in the clinical effectiveness study determined that florfenicol and terbinafine hydrochloride inhibit the growth of bacteria and yeast commonly associated with otitis externa in dogs. No consistent synergistic or antagonistic effect of the two antimicrobials was demonstrated. The addition of mometasone furoate to the combination did not impair antimicrobial activity to any clinically significant extent.

In a field study (see **EFFECTIVENESS**), at least 10 isolates from successfully treated cases were obtained for *S. pseudintermedius* and *M. pachydermatis*.

EFFECTIVENESS:

In a well-controlled, double-masked field study, CLARO® was evaluated against a vehicle control in 221 dogs with otitis externa. One hundred and forty six dogs were treated with CLARO® and 75 dogs were treated with the vehicle control. All dogs were evaluated for safety. Treatment (1 mL) was administered once on Day 0 to the affected ear(s). Prior to treatment, the ear(s) was cleaned with saline. The dogs were evaluated on Days 0, 7, 14, and 30. Blood work and urinalysis were obtained on Day 0 pre-treatment and Day 30 at study completion. Four clinical signs associated with otitis externa were evaluated: erythema, exudate, swelling, and ulceration. Success was based on clinical improvement at Day 30. Of the 183 dogs included in the effectiveness evaluation, 72.5% of dogs administered CLARO® solution were successfully treated, compared to 11.1% of the dogs in the vehicle-control group (p=0.0001).

ANIMAL SAFETY:

In a target animal safety study, CLARO® was administered aurally to 12-week-old Beagle puppies (4 dogs/sex/group) at 0X, 1X, 3X, and 5X the recommended dose once every 2 weeks for a total dosing period of 28 days (3 times the treatment duration). No clinically relevant treatment-reled findings were noted in hearing tests, body weight, weight gain, or food consumption. CLARO® administration was associated with post-treatment ear wetness or clear aural exudate, increased absolute neutrophil count, decreased absolute lymphocyte and eosinophil counts, suppression of the adrenal cortical response to ACTH-stimulation, decreased adrenal weight and atrophy of the adrenal cortex, increased liver weight with hepatocellular enlargement/cytoplasmic change, and decreased thymus weight. Other potentially treatment-related effects included mild changes to AST, total protein, inorganic phosphorus, creatinine, and calcium.

STORAGE INFORMATION:

Store between 20°C-25°C (68°F-77°F), excursions permitted 15°C-30°C (59°F-86°F).

HOW SUPPLIED:

 ${\sf CLAR0}^{\circ}$ solution is supplied in a single-use dropperette in a blister. Each dropperette contains one 1 mL dose.

CLARO® is available in cartons of two, ten, or twenty dropperettes.

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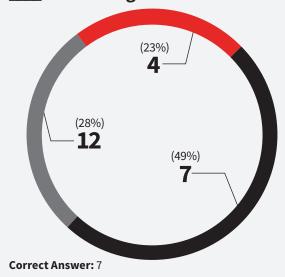




From Clinician's Brief on Social Media

WE ASKED ...

The most sensitive period for feline socialization ends at approximately weeks of age.



What is your least favorite surgical procedure?

"Anything that involves a brachycephalic."—Nichola W

29 🕝 4 🐸

"Cat dental extractions."—Stefan C

36 🖰 4 🐸

"Colon evacuation in an obese bulldog that has not had a bowel movement in over a week."—Brianne B

10 🕜 2 😝 4 😯

"Deep-chested, fat dog spays ... One of the reasons I became a cat specialist."—Kelly S

5 🕝 3 🐸

"All of them!"—Tina K

21 6 1 0 2 😜



Tell us your most clever patient names.

"Had a client who lost his beloved cat named Bob; came in a few weeks later with his new cat 'Not Bob.'"—Kimber S

10 🕜 8 🐸

"I named a black stray cat that came in with a rotated displaced shoulder blade 'Count Scapula.'"—Julie N

32 🕜 5 🔿 9 😝

"Nothing beats 'Ozzy Pawsborne,' the king of barkness." —Alexandra P

29 🗸 2 🗘 5 🐸 1 😯

"A cat named Jesus ... because when he was a kitten, he was always under their feet, and when they would trip over him, they would exclaim 'Jesus!'"-Elizabeth D

10 🕝 4 🐸

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18% Always

25% Usually

40% Rarely

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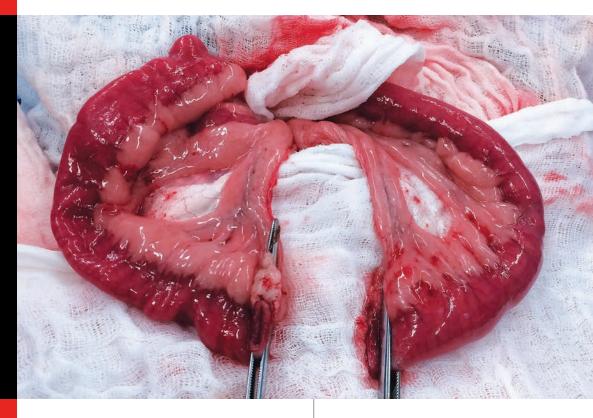
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ANESTHESIA OPTIONS

Anesthetic Management in a Hyperthyroid Cat

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OUR AUTHORS



KIKO E. BRACKER, DVM, DACVECC, is a director of the emergency and critical care and anesthesia services at Angell Animal Medical Center in Boston, Massachusetts, where he has worked as a staff criticalist for 12 years.

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MARJORIE L. CHANDLER, DVM, MS, MANZCVS, DACVN, DACVIM, MRCVS, is a small animal nutrition consultant at Vets Now Referrals in Glasgow, Scotland, and a private consultant in small animal internal medicine and clinical nutrition. She earned her DVM from Colorado State University and is co-chair of the WSAVA Global Nutrition Committee and WSAVA liaison to the American Academy of Veterinary Nutrition. Dr. Chandler is a member of the WSAVA Dental Standardization Project Committee and a charter member and founder of the European Veterinary Nutrition Educators Group. She is also on the scientific advisory board for the European Pet Food Industry Federation.

DIET IN DISEASE PAGE 63



THOMAS CHEN, DVM, MS, DACVO, is an assistant professor at University of Tennessee, where he also earned his DVM. He completed a small animal internship and comparative ophthalmology residency at Colorado State University. Dr. Chen is interested in all aspects of clinical ophthalmology but enjoys treatment of cataract and corneal disease.

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DANIEL J. LOPEZ, DVM, is currently completing a surgical residency at Cornell University. He completed an internship at University of Guelph.

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ANANSA PERSAUD, DVM, is currently completing a rotating internship at Long Island Veterinary Specialists in Plainview, New York. She earned her DVM from Saint George's University and enjoys volunteering for the Wildlife Conservation.

CLINICAL VIEW PAGE 35



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The safe use of ENTYCE has not been evaluated in dogs used for breeding or pregnant or lactating bitches.

Adverse Reactions: Field safety was evaluated in 244 dogs. The most common adverse reactions were diarrhea and vomiting. Of the dogs that received ENTYCE (n = 171), 12 experienced diarrhea and 11 experienced vomiting. Of the dogs treated with placebo (n = 73), 5 experienced diarrhea and 4 experienced vomiting.

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AT2-021-16 August 2016





(capromorelin oral solution

IMPORTANT SAFETY INFORMATION: ENTYCE® (capromorelin oral solution) is for use in dogs only. Do not use in breeding, pregnant or lactating dogs. Use with caution in dogs with hepatic dysfunction or renal insufficiency. Adverse reactions in dogs may include diarrhea, vomiting, polydipsia, and hypersalivation. Should not be used in dogs that have a hypersensitivity to capromorelin. Please see the full Prescribing Information for more detail. See page 10 for product information summary.



LISA M. POHLMAN, DVM, MS, DACVP, is an associate professor at Kansas State University. She earned her DVM from University of Guelph and, after 3 years in small animal practice, completed a residency and earned her master's degree in clinical pathology from Auburn University. Dr. Pohlman is an active teacher and mentor of veterinary students, interns, residents, and graduate students and enjoys providing CE in clinical pathology through speaking engagements, online courses, and publications. She also serves as the medical director of the Riley County Humane Society in Manhattan, Kansas.

COMPARATIVE IMAGERY PAGE 70



AMEET SINGH, DVM, DVSc, DACVS (Small Animal), is an associate professor and small animal surgeon at University of Guelph, where he also completed a small animal rotating internship and surgical residency and earned his DVSc. Dr. Singh earned his DVM from Atlantic Veterinary College. His primary research interests include surgical site infections and minimally invasive surgery.

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DANIEL D. SMEAK, DVM, DACVS, is a professor and chief of surgery at Colorado State University. His research interests include development and assessment of innovative methods to train students and residents in core surgical skills, as well as investigating a wide range of soft tissue surgical conditions. He remains active in the soft tissue surgery specialty practice at his institution, and he enjoys delivering interactive CE lectures and wet laboratories to veterinarians worldwide.

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LIORA WALDMAN, BVM&S, CertSAD, MRCVS, is the owner of a small animal dermatology and allergy clinic in Haifa, Israel. She earned her veterinary degree from Royal Veterinary School in Edinburgh, Scotland, and was certified in small animal dermatology from Royal Veterinary College in London. Dr. Waldman has worked as a second opinion dermatologist in High Wycombe, Tel Aviv, and Haifa.

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CRAIG B. WEBB, PhD, DVM, DACVIM, is the head of the small animal medicine section at Colorado State University Veterinary Teaching Hospital. Dr. Webb's clinical specialty is gastroenterology and hepatic disease. He coteaches CE laparoscopy courses and has been published on copper-associated hepatopathy in Dalmatians, the use of S-adenosyl methionine to treat acetaminophen toxicity in cats, and laparoscopic diagnosis of pancreatitis. Dr. Webb frequently presents on the use of nutraceuticals and antioxidants in liver disease and the use of probiotics in chronic GI disease.

TOP 5 PAGE 75



ALEXANDER WERNER, VMD, DACVD, is the editor of the dermatology section of the 5-Minute Veterinary Consult textbook and coauthor of the second edition of Small Animal Dermatology Clinical Companion, as well as the upcoming third edition. He practices at the Animal Dermatology Center in Studio City and Westlake Village, California, and Reno, Nevada. Dr. Werner serves on the Clinician's Brief advisory board.

TOP 5 PAGE 29





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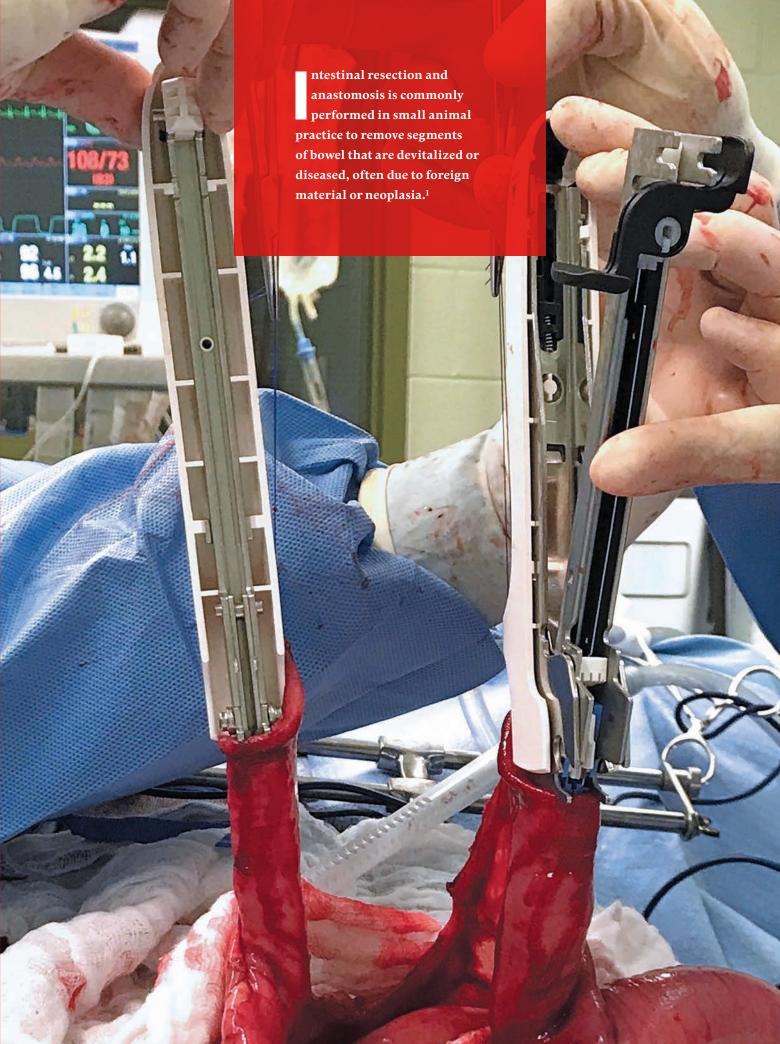
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LINEAR-STAPLED GASTROINTESTINAL ANASTOMOSIS

Daniel J. Lopez, DVM *Cornell University*

Ameet Singh, DVM, DVSc, DACVS (Small Animal)
University of Guelph

Daniel D. Smeak, DVM, DACVS Colorado State University



In human and veterinary medicine, stapling devices have been developed for GI surgery, and a variety of different stapling techniques for intestinal anastomosis have been described, including¹⁻¹⁰:

- ► Everting, triangulating end-to-end anastomosis (EEA) using a thoracoabdominal linear stapler
- ▶ Inverting EEA using an EEA circular stapler
- ▶ EEA using a skin stapler
- ► Antiperistaltic side-to-side (ie, functional end-to-end) anastomosis using a GI anastomosis (GIA) linear and/or cutting stapler

Stapled GIA in dogs and cats and, more recently, a technique in dogs for a stapled functional end-to-end anastomosis (SFEEA) using only a GIA stapler have also been reported. ^{10,11} Ideally, SFEEA is used following enterectomy of the jejunum and/or ascending duodenum based on the mobility of this portion of the small intestine. Other portions of the intestine (eg, duodenum, large intestine)

Ideally, stapled functional end-to-end anastomosis is used following enterectomy of the jejunum and/or ascending duodenum based on the mobility of this portion of the small intestine.

DST = directional stapling technology

EEA = end-to-end anastomosis

GIA = gastrointestinal anastomosis

SFEEA = stapled functional end-to-end anastomosis

are more fixed because of the short mesentery, precluding the use of this technique.

Studies have been conducted to evaluate the technique and outcome of SFEEA in veterinary medicine.1,12-14 Potential benefits of SFEEA as compared with hand-sewn anastomosis include reduced procedure time, decreased tissue trauma, decreased intraoperative contamination, consistency and repeatability of the anastomosis, and preservation of blood supply. 13-15 In addition, severe luminal disparity between 2 cut bowel ends (eg, severe segmental dilation orad to an obstructive foreign body) can be readily resolved via SFEEA. A multi-institutional retrospective study in dogs demonstrated no significant difference in anastomosis dehiscence rates or decreased procedure time with SFEEA as compared with hand-sewn anastomosis.¹²

Disadvantages of SFEEA as compared with hand-sewn anastomosis include the learning curve required to perform the procedure and the inability to perform this procedure in areas of the GI tract other than the jejunum and ascending duodenum. An additional limiting factor of stapled anastomosis may be financial investment, with SFEEA instruments and staple cartridges costing 15 to 25 times more than suture costs. However, in some institutions, the total procedural time saved may result in equivalent overall costs between SFEEA and hand-sewn anastomosis.

Preoperative peritonitis, a serum albumin concentration less than 2.5 g/dL, and presence of an intestinal foreign body are classically reported risk factors for intestinal anastomosis dehiscence following hand-sewn anastomosis. ¹⁶ In a retrospective study examining risk factors specifically related to SFEEA dehiscence, preoperative presence of inflammatory bowel disease, intraoperative hypotension, and resection and anastomosis involving the large intestine were identified as risk factors. ¹⁴

Preoperative peritonitis was examined and was not an identified risk factor for SFEEA, contrary to previous reports. ¹⁴ Furthermore, in another retrospective study, SFEEA was found to be less likely to undergo dehiscence as compared with hand-sewn intestinal anastomosis in dogs with preoperative septic peritonitis. ¹

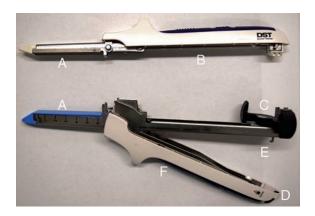
With proper instruction, SFEEA has been demonstrated to be a reliable tool for surgeons and may be useful during emergency situations to decrease operative time in unstable patients when a rapid anastomosis is required and to potentially decrease dehiscence risk in patients with septic peritonitis. ^{13,14}

SURGICAL STAPLER FUNCTIONALITY

Before performing a linear-stapled intestinal anastomosis, the surgeon should become familiar with the GIA stapling device used for SFEEA (*Figure 1*). The GIA stapler is a linear/cutting stapling device composed of 2 interlocking halves. When fired via a pushbar handle, the device applies 4 staggered rows of B-shaped titanium staples while a knife blade cuts between the 2 rows of double staple lines (*Figure 2*). The knife blade stops cutting approximately 8 mm before the last staple at the tip of the fork.

Staple cartridges for the directional stapling technology (DST) series GIA stapler come in different lengths and closed staple heights. The color of the cartridge corresponds to the closed staple height. Blue staple cartridges (1.5-mm closed staple height) are typically used in small animals for SFEEA. White (1-mm closed staple height) and green (2-mm closed staple height) staple cartridges are also available but are not routinely used for SFEEA.

With proper instruction, stapled functional end-to-end anastomosis has been demonstrated to be a reliable tool.^{1,13,14}



▲ FIGURE 1 A DST series GIA 60 stapler. Stapler forks (A), stapler handle (B), push trigger (C), release mechanism (D), locking mechanism (E), cartridge lock lever (F; a blue cartridge is loaded in the opposite side of the handle)



▲ FIGURE 2 A GIA 60 stapler with a blue cartridge staple pattern. Four staggered staple rows, with a slot between staple rows 2 and 3 for the cutting blade to pass through, can be seen. The cutting blade (white arrow) is covered by a protective plastic sheath.

WHAT YOU WILL NEED

- ► Standard surgical instrument kit
- ► Balfour retractor
- ► GIA stapler (60-mm and/or 80-mm or 100mm for mediumto-large-breed dogs) and blue staple cartridges that correspond in length to the stapler
- Doyen intestinal forceps (atraumatic; 2 pairs)
- ► DeBakey thumb forceps (2 pairs)
- ► Traumatic forceps (eg, Rocheter-Carmalt; 1 pair)
- ► Suture material (3-0 monofilament, absorbable)

STEP-BY-STEP STAPLED FUNCTIONAL **END-TO-END ANASTOMOSIS**

STEP 1

Anesthetize the patient and place in dorsal recumbency. Administer antimicrobial therapy (eg, cefoxitin [30 mg/kg IV for clean-contaminated surgery]) 30 minutes before incision and every 90 minutes thereafter until skin closure; of note, recent data suggest that q4h administration of cefoxitin is also acceptable.¹⁷ Clip, prepare, and drape the ventral abdomen for aseptic surgery.

Perform a ventral midline exploratory laparotomy and remove the falciform ligament to improve abdomen exposure, then place a Balfour retractor. Explore the abdomen thoroughly in a systematic fashion, and isolate the affected intestinal segments with multiple layers of saline-soaked laparotomy sponges. Perform an enterectomy and, if indicated, submit for histopathologic evaluation.

Author Insight

An initial pair of Doyen forceps (gripping the portion of bowel to remain intact) can help with intestinal manipulation and resection and anastomosis, and traumatic forceps (gripping the portion of bowel to be removed) can help limit surgical-site contamination. When placing Doyen forceps, only one ratchet should be used to prevent devitalization of tissue. Although the initial Doyen forceps are placed at the traditional site of hand-sewn anastomosis, this portion of tissue will be removed after SFEEA completion.

STEP 2

After resecting the affected intestine, milk the intestinal contents orally and aborally to the Doyen forceps (A). Place a second pair of Doyen forceps approximately 10 cm orally and aborally to the first set of Doyen forceps (B). This technique is employed to minimize contamination when using the stapling devices for anastomosis, as the initially placed pair of forceps will be removed on staple application.





▲ Proximal and distal segments of the jejunum occluded by Doyen forceps at the site of resection (A). The resected portion of the intestine was removed from the surgical site with Rochester-Carmalt (ie, traumatic) forceps attached (not pictured). Proximal and distal jejunal segments of the intestine with second Doyen forceps placed approximately 10 cm away from the initial Doven forceps (B; black arrows)

GIA = gastrointestinal anastomosis SFEEA = stapled functional end-to-end

STEP 3

Place 2 stay sutures (eg, 3-0 polydioxanone) into the cut ends of each intestinal segment on the mesenteric border. Once the stay sutures have been applied, remove the first pair of Doyen forceps directly at the cut bowel ends; leave the second pair in place until the stapled anastomosis is complete. Use the stay sutures to elevate the bowel ends and to facilitate insertion of each fork of the GIA stapler (A). It is important to ensure symmetrical apposition of the antimesenteric border of the intestine before locking the stapler. The authors recommend apposition of the antimesenteric borders of the bowel because this can help minimize incidence of trauma to the vascular supply on the mesenteric border.

When placement is deemed adequate, lock and fire the forks, creating the side-to-side opening between the bowel lumens (*B*). After firing, disengage and remove the forks. Carefully inspect the anastomosis site to ensure proper staple placement, which is dependent on passage of the staple fully through both layers of the adjacent intestinal wall and on consistent closure of the B-shaped staple on the opposite tissue edge.



Two stay sutures have been placed at the mesenteric border of the jejunum, and the initially placed Doyen forceps have been removed (A). The stay sutures are elevated to allow for insertion of the individual forks of the GIA stapler into the lumen of both jejunal ends. The GIA stapler is engaged and locked, ensuring symmetrical apposition of the antimesenteric border and terminal end of the jejunum (B). The GIA stapler is then fired. The stay sutures (black arrows) can be noted.



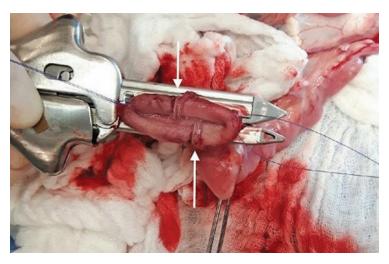
Author Insights

Caution should be exercised when using this stapling technique for anastomosis in cases in which the intestinal wall is severely thickened (eg, inflammatory bowel disease), as the closed blue cartridge staple leg length (1.5 mm) may not be long enough to completely capture both intestinal walls. ¹⁴ In cases of severely thickened intestines, hand-sewn anastomosis is recommended.

Future obstruction at the site of anastomosis is a potential long-term risk, with one report documenting subsequent obstruction in 4.3% of SFEEAs. The authors routinely use a GIA 60 stapler for the first half of the SFEEA; in their clinical experience, a GIA stapler of longer working length, although not harmful, does not appear to be beneficial in preventing subsequent obstruction. Further investigation in this area is needed.

STEP 4

Using the previously placed stay sutures for handling the intestinal segments, place the GIA stapler (with a new loaded cartridge) perpendicular to the lumen of the intestine. Before locking, offset the staple rows from the lumens portion using 2 pairs of DeBakey thumb forceps. This prevents the initial staple lines from being stacked on top of each other, which could prevent complete engagement of the staples through both walls of the terminal end of the SFEEA. Lock and fire the stapler. The authors generally aim to leave 1 mm to 3 mm of tissue beyond the edge before firing the GIA stapler. The GIA stapler will automatically transect the bowel, resulting in a 2-row stapled edge creating the "waist." The remaining tissue at the terminal end of the SFEEA does not need to be oversewn.



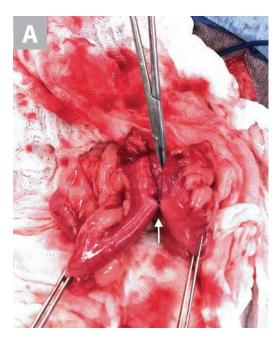
▲ The 2 previously placed stay sutures are gently distracted to maintain tension on the intestine. A GIA stapler (of appropriate length) is engaged and locked over the terminal end of the intestine. Approximately 3 mm of tissue extends beyond the proposed staple line, and no tissue extends past the 0 mark of the GIA stapler, ensuring a complete terminal seal. If tissue extends past the 0 mark of the GIA stapler, a stapler of longer working length should be used. The stapler is fired, resulting in a stapled terminal end of the intestine and transection of the remaining distal portion, including the stay sutures. The 2 staple lines of the GIA line should be offset (white arrows) to ensure staple engagement of all tissues.

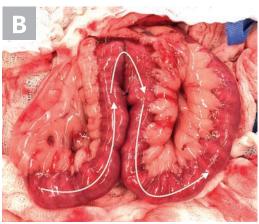
Author Insight

The GIA 60 stapler is often too short to adequately engage all tissues when closing the terminal end of the SFEEA in medium-to-large-breed dogs; in such patients, a GIA 80, 90, or 100 stapler is recommended.

STEP 5

Two simple interrupted, prolonged absorbable monofilament sutures should be placed just below the base (ie, point of the "V" intersecting GIA staple line) of the anastomosis to minimize tension on the staple line (A). These sutures should aim to capture submucosa for holding power (B).





▲ Two simple interrupted, prolonged absorbable monofilament sutures are placed at the SFEEA base (A; white arrow) to minimize tension on the staple line. Completed SFEEA, with a demonstration of the flow of ingesta through the SFEEA (B; white arrows)

STEP 6

Remove the laparotomy sponges from the surgical field. With a new pair of sterile surgery gloves, use a separate sterile closure pack to complete the laparotomy. Lavage the abdomen thoroughly with sterile saline. Using a monofilament absorbable suture, close the mesenteric defect in either an interrupted, cruciate, or continuous pattern. Avoid damaging adjacent vasculature supplying the anastomosed bowel in the mesentery. Drape the omentum over the anastomosis site before closing the abdominal incision in a routine fashion, and perform a routine closure of the abdomen.

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GIA = gastrointestinal anastomosis

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Advances in Wound Management

Negative-pressure wound therapy (NPWT; ie, vacuum-assisted wound closure) uses local negative pressure to promote wound healing. Benefits include removal of interstitial fluid, increased local circulation and bacterial clearance, improved granulation tissue formation and free graft acceptance, and more rapid wound closure. NPWT bandages consist of sterile foam or gauze over the wound or graft, suction tubing, adherent film, and a regulated negative-pressure drainage device. NPWT is contraindicated in wounds that contain neoplastic cells, as this technique may increase blood flow and cellular proliferation.

Therapeutic lasers—referred to as low-level or cold lasers because they have an output of less than 500 milliwatts—typically have wavelengths in the infrared or red spectrum and

cannot cut tissue. Benefits include vasodilation, angiogenesis, increased collagen synthesis, leukocyte stimulation, differentiation of fibroblasts into myofibroblasts, and enhanced antioxidant effects, all of which contribute to improved tissue healing, wound contraction, increased strength of repaired tissue, improved immune function, protection against ischemia and reperfusion injury, and decreased pain sensation. Although physiologic effects of therapeutic lasers have been documented, outcomes differ, likely due to variations in laser parameters, making extrapolation of results between individual studies difficult.

Extracorporeal shock wave therapy is an acoustic energy modality similar to but more intense than ultrasonography. Its exact mechanism of action is not fully understood but is believed to increase cytokine and growth factor expression through mechanical stimulation of cells. It has been used to treat chronic tendinopathies, delayed and nonunion fractures, chronic wounds, and osteoarthritic pain.—*Shaw KK*

Hypotensive Resuscitation

Hemorrhage and hypovolemia secondary to trauma are important and relatively common causes of morbidity and mortality in veterinary patients. Fluid resuscitation at shock dosages has traditionally been used to quickly restore vascular fluid volume and maintain normal blood pressure. However, studies in human medicine have shown that hypotensive resuscitation (ie, administration of small volumes of fluid to maintain a subnormal blood pressure) may provide a better outcome and less hemorrhage than traditional fluid

resuscitation. By maintaining permissive hypotension in this manner, it is possible to avoid a rapid increase in intravascular hydrostatic pressure and blood pressure that occurs with traditional fluid resuscitation measures and thereby limit the dislodging of protective blood clots and prevent further hemorrhage. A target mean arterial pressure greater than 60 mm Hg can provide adequate CNS perfusion while decreasing the possibility of rebleeding. Hypotensive resuscitation is most useful in patients for which definitive hemorrhage control is readily available. A clinical application of hypotensive resuscitation would be in a patient with hemoperitoneum from a ruptured abdominal mass that receives conservative fluid boluses over longer periods of time (eg, 10 mL/kg over 30 minutes vs the traditional 20 mL/kg over 15 minutes).—Culler C

Luxations: How to Approach & When to Refer

Trauma is the most common cause of luxations in pets. Although nonsurgical treatment is possible, many patients require surgery. Preservation of the normal functioning joint is the goal for most luxations, and owner education and compliance are key.

Shoulder luxations are uncommon. Rest and treatment with NSAIDs may be adequate for occasional congenital cases, but a surgical salvage procedure is advised in cases of persistent lameness. Traumatic injuries that occurred 3 to 5 days before presentation with no fractures present may be stabilized with closed reduction followed by 10 to 14 days of immobilization. Open reduction is recommended in patients with failed closed reductions, unstable or chronic luxations, or fractures.

Blunt trauma is the cause of most elbow luxations. Closed reduction within the first few days followed by spica splint immobilization for 2 weeks is often successful. Collateral ligament stability should be assessed after reduction. Surgical referral is recommended in patients with chronic injuries, avulsion fractures, collateral ligament injuries, or residual instability.

Carpal luxations and/or subluxations typically occur following acute or

repeated injury, although endocrine disease can lead to ligamentous laxity and degeneration. Arthrodesis and/or ligamentous repair are often required. Splints or external coaptive devices are unlikely to result in long-term stability. The same is true for most tarsal luxations and/or subluxations.

Most coxofemoral luxations result from trauma and are craniodorsal. Closed reduction under general anesthesia can produce good outcomes in acute cases with no fractures and good hip conformation. Reduction is followed by 2 weeks in an Ehmer sling. In patients with failed closed reduction, adjacent fractures, poor hip conformation, or multiple limb injuries, open reduction or salvage procedures are recommended.—*Robinson DA*

Update: Gastric Dilatation-Volvulus

Giant- and large-breed dogs have up to a 21.6% and 24% likelihood, respectively, of developing gastric dilatation-volvulus (GDV). Risk factors include age, breed, first-degree relative, behavioral tendencies, and dietary factors. However, relatively little is known regarding the etiology of GDV. The canine GI tract is a physiologically complex system that is affected by numerous internal and external factors, including the nervous and endocrine systems as well as diet and microbiome. Research in humans has indicated that

the microbiome can affect various conditions (eg, obesity, Crohn's disease, celiac disease, autism, kidney disease). More reports are becoming available on the canine microbiome and metabolome, and a potential link between inflammatory bowel disease and GDV has been found.

Research has indicated that dogs with naturally occurring GDV have different GI motility patterns than dogs with experimentally induced GDV, including changes in contractions controlled by the hormones motilin and ghrelin. This study investigated

the association between ghrelin activity and GDV, gastric motility, and motilin in various breeds and aimed to determine the time to gastric emptying of a nondigestible solid (ie, a wireless motility device) in dogs that had and had not experienced GDV; thus, it was important to determine if gastropexy affected the passage of the wireless motility device. Results indicated that prophylactic gastropexy did not negatively affect gastric emptying time or passage of the wireless motility device. Future research will continue to focus on GDV as part of a complex GI syndrome.—Nelson LL

Giant- and large-breed dogs have up to a 21.6% and 24% likelihood, respectively, of developing gastric dilatation-volvulus.

Surgical Oncology Update

Studies have shown that clean histologic margins can result in decreased local recurrence and prolonged survival. Pathologic margin assessment ideally includes quantitative value (eg, 5 mm from cut edge) and qualitative description (eg, normal skeletal muscle).

Canine mast cell tumor (MCT) recurrence rates reportedly relate to grade, mitotic index, and tumor size, with tumors larger than 3 cm increasing the chance for recurrence. Improved outcomes are often reported with histologically complete margins, which have been achieved in 91% to 100% of grade I and II canine MCTs using 2-cm lateral and 1 fascial plane deep margins. For known grade III MCTs, 3-cm lateral margins and 1 fascial plane deep

are recommended; however, recurrence rates as high as 36% have been reported with histologically clean margins. Improved survival is achieved by removing the primary tumor. Canine soft tissue sarcomas should have 2- to 3-cm lateral and 1 fascial plane deep margins. Low-, intermediate-, and high-grade recurrence rates after surgical excision are 7%, 34%, and 75%, respectively, and are associated with a fivefold increased risk for tumor-related death; thus, curative surgical intent is warranted. Canine oral squamous cell carcinoma, fibrosarcoma, and malignant melanoma almost always require removal of mandibular or maxillary bone for complete surgical excision; recommended margins are 2 cm.

Feline injection site sarcomas are very locally aggressive. Recent recommendations are for 5-cm lateral margins and 2 fascial planes deep; recurrence rates using these margins is 14%.

Surgical recommendations to prevent

tumor seeding include changing gloves and instruments before closure of surgical sites where there was contact of neoplastic cells. Studies have supported removal of metastatic lymph nodes, as this can lead to improved survival with many tumor types.—Lux CN

Canine mast cell tumor recurrence rates reportedly relate to grade, mitotic index, and tumor size, with tumors larger than 3 cm increasing the chance for recurrence.

Treating Trauma to the Eye

Periocular trauma is common in cats and dogs. Proptosis (ie, globe prolapse) can occur relatively easily in brachycephalic breeds, but management is typically straightforward. Proptosis in nonbrachycephalic breeds usually occurs with more significant trauma. Immediate treatment should include keeping the cornea moist with ophthalmic lubricant or saline-soaked cotton. Owners of brachycephalic dogs with acute prolapse may be instructed to replace the globe with gentle pressure. On examination,

the prolapsed globe should be checked for corneal or scleral rupture, hyphema, or intraocular damage; pupillary and dazzle reflexes should be assessed. If the extraocular tissues appear intact and there is no sign of severe intraocular damage, the globe should be reduced and a temporary tarsorrhaphy performed.

Sharp penetrating trauma to the globe cavity (eg, from sticks and bones) may occur from various directions, including the oral cavity. Patients with penetrating corneal wounds should be handled extremely carefully to avoid globe rupture during examination. Corneal lacerations should be carefully cleaned with saline solution, gently

debrided, and repaired with fine suture (eg, 8-0 or 9-0 polyglactin 910). Lens removal (ie, phacoemulsification) may be indicated if the lens capsule is involved.

Compressive blunt trauma to the globe can result in serious damage and permanent vision loss. The patient should be assessed for discharge, hemorrhage, direct and consensual pupillary responses, and dazzle and menace responses. Findings may include lens displacement, corneal or scleral rupture, hemorrhage, or retinal detachment. Ocular ultrasonography can be a helpful tool, especially when intraocular structures cannot be well visualized.—Petersen-Jones SM

LONE STAR TICKS

RISK TO DOGS, RISK TO HUMANS.

BRIAN HERRIN

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SCOTT COMMINS

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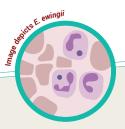
THOMAS MATHER

BS, MS, PhD, University of Rhode Island



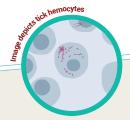
LONE STAR TICKS CAN TRANSMIT PATHOGENS.

While ticks are certainly an unpleasant sight for pet owners, hygiene is far from the primary concern. Lone star ticks can carry several pathogens that may be transmitted to the host during feeding. It's important to have a standardized plan throughout your clinic for prevention, diagnosis and treatment of each tick-borne disease.



EHRLICHIA SPP.

Lone star ticks can transmit both *E. ewingii* and *E. chaffeensis*. In-house antibody tests do not distinguish between *E. canis* and other species. Consider clinical signs and CBC/ platelet count to help determine if there is an active infection before making treatment decisions.



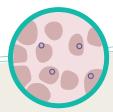
RICKETTSIA SPP.

While lone star ticks have been shown to carry *R. amblyommii* and *R. montanensis*, they have also been shown to infrequently transmit *R. rickettsia*, which causes Rocky Mountain spotted fever.¹ Antibody tests can't distinguish between these three pathogens, so clinical signs are very important to help diagnose Rocky Mountain spotted fever. Antibiotic therapy should not be delayed in a patient with signs suggestive of Rocky Mountain spotted fever.



STARI

Southern Tick-Associated
Rash Illness (STARI) is
associated with the feeding
of lone star ticks, although
the causative agent is
unknown. STARI mimics
the target lesion
of Lyme disease in humans
but is not known to cause
clinical disease in pets.



CYTAUXZOON FELIS

This feline pathogen can lead to potentially fatal disease. Infected cats may be jaundiced and painful on splenic palpation. Diagnosis can be confirmed with blood tests.

RED MEAT ALLERGIES: A UNIQUE RISK FOR HUMANS.

A 2009 study linked a series of allergic reactions in Virginia and Missouri to consumption of red meat.² Patients who had eaten red meat without a problem in the past now developed symptoms 3 to 6 hours after meat ingestion.

Comparison of geographical distribution of red meat allergy cases, tick-borne diseases, and tick distribution suggested a connection between lone star tick bites and red meat allergies.



ALPHA-GAL

Galactose-α-1,3-galactose
(alpha-gal) is a carbohydrate
normally present in the tissues
of most mammals (except for
humans and apes). After being bitten by a lone
star tick, some individuals develop an allergic
immune response to alpha-gal. A person who
develops this allergy can have a severe
reaction after ingesting red meat. Thus, the

common name for this condition is "red meat allergy," or sometimes "alpha-gal syndrome." Blood tests have been used to identify patients with this allergy.

5 THINGS TO KNOW ABOUT LONE STAR TICKS.

Thomas N. Mather, PhD, Professor and Director, University of Rhode Island Center for Vector-Borne Disease and its Tick

Resource Center, offers five unique facts about the lone star tick.



LONE STAR TICKS ARE FAST.

Lone star ticks move very quickly and will run aggressively toward a host. Compared to other ticks, they scramble quickly through fur or up a pant leg. Tick checks are very important, even if the pet has only been outside briefly.



LONE STAR TICKS ARE COMMONLY MISIDENTIFIED.

Steps to confirm a lone star tick:

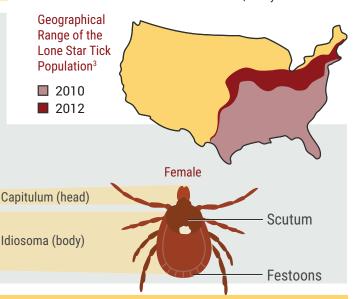
- Narrow your vision to just the scutum (or shield)
- Check for the distinctive white spot (or "lone star") which identifies the adult female lone star tick

 Male
- The adult male lacks the white spot but typically has spots or streaks of white around the outer edge of the body



LONE STAR TICKS ARE EXPANDING THEIR RANGE.

Information gathered from the TickSpotters program indicates that lone star ticks are spreading into the Upper Midwest. Dr. Mather suggests that the spread of this tick species is related to the increased abundance and suburbanization of white-tailed deer, a key host.





LONE STAR TICKS DO NOT TRANSMIT LYME DISEASE.

In a study testing more than 22,500 lone star tick specimens, there was no measurable prevalence of *Borrelia burgdorferi*. This may be partly because this tick species rarely attaches to white-footed mice, the primary reservoir of *B. burgdorferi*, but favors white-tailed deer, an animal rarely infectious for the Lyme disease germ. It could also be related to potentially borreliacidal properties of lone star tick saliva.



LONE STAR TICK LARVAE ARE TINY.

The larvae are so small they can crawl right through the fabric of socks! Wearing permethrin-treated clothing can help prevent bites. Look out for tiny, poppy seed-sized engorged larvae especially on pet's feet, or wandering loose in homes.

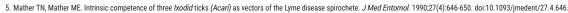
LONE STAR TIPS:

- Make a plan to handle tick-borne diseases in your clinic – Don't be caught surprised!
- If treatment fails initially, consider the possibility of a co-infection with several pathogens.
- Prevention is key.

References

- References

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GALLIPRANT® (grapiprant tablets)

For oral use in doas only

20 mg, 60 mg and 100 mg flavored tablets

A prostaglandin E. (PGE.) EP4 receptor antagonist; a non-cyclooxygenase inhibiting, non-steroidal anti-inflammatory drug

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

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

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

The dose of GALLIPRANT (grapiprant tablets) is 0.9 mg/lb (2 mg/kg) once daily. GALLIPRANT tablets are scored and dosage should be calculated in half tablet increments. Dogs less than 8 lbs (3.6 kgs) cannot be accurately dosed. See product insert for complete dosing and administration information.

Contraindications: GALLIPRANT should not be used in dogs that have a hypersensitivity to grapiprant. Warnings: Not for use in humans. Keep this and all medications out of reach of children and pets. Consult a physician in case of accidental ingestion by humans. For use in dogs only. Store GALLIPRANT out of reach of dogs and other pets in a secured location in order to prevent accidental ingestion or overdose.

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

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

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

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

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

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

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

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

^{*}Dogs may have experienced more than one type or occurrence during the study. GALLIPRANT was used safely during the field studies with other concurrent therapies. including antibiotics, parasiticides and vaccinations.

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

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

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

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

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

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



NADA 141-455, Approved by FDA US Patents: 6,710,054; 7,960,407; 9,265,756

Made in New Zealand Manufactured for: Aratana Therapeutics, Inc., Leawood, KS 66211 Reference: 1. http://www.vet.upenn.edu/docs/default-source/VCIC/canine-bpi_userguide.pdf?sfvrsn=0

Additional information is available at 1-888-545-5973.

GALLIPRANT is a trademark of Aratana Therapeutics, Inc.

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Brief Summary: AT1-040-16

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 antiinflammatory drugs, such as COX-inhibiting NSAIDs or corticosteroids, should be avoided. Concurrent use with other anti-inflammatory drugs or proteinbound drugs has not been studied. The safe use of Galliprant has not been evaluated in dogs younger than 9 months of age and less than 8 lbs (3.6 kg), dogs used for breeding, pregnant or lactating dogs, or dogs with cardiac disease. The most common adverse reactions were vomiting, diarrhea, decreased appetite, and lethargy. Please see brief summary to the left for full prescribing information.

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PRESCRIBE GALLIPRANT® (grapiprant tablets) FROM THE EARLIEST DIAGNOSED STAGES OF OSTEOARTHRITIS (OA).

Galliprant is a first-in-class, non-COX-inhibiting prostaglandin receptor antagonist (PRA) that specifically acts on the EP4 receptor. Its mode of action targets OA pain and inflammation while reducing the impact on GI, kidney and liver homeostasis.^{1,2} It was well-tolerated by healthy dogs in a 9-month safety study at up to 15 times the recommended therapeutic dose.^{2,3}

Visit galliprantfordogs.com/early for more information about Galliprant.

INDICATION

Galliprant is indicated for the control of pain and inflammation associated with osteoarthritis in dogs. See page 26 for product information summary.



X ARATANA



Evaluating the Skinny Kitty

Cyndie Courtney, DVM Sponsored by Dechra Veterinary Products

The Case

Peanut was a 12-year-old spayed female domestic shorthair cat. She was recently diagnosed with hyperthyroidism and elevated liver enzymes after being presented with vocalization and weight loss, despite a good appetite.

For a full discussion of presentation, history, and diagnostics, visit **cliniciansbrief.com/ dechra-hyperthyroidism**.

Treatment

A variety of treatment options exist for hyperthyroidism. The owners elected to treat with methimazole because of their pet's advanced age, cost limitations, desire for rapid response to treatment, and complications with feeding multiple cats in the household. FELIMAZOLE® (methimazole) Coated Tablets are the only FDA-approved treatment for managing feline hyperthyroidism.³ Peanut was started at the approved initial dose of 2.5 mg q12h PO.⁴

Monitoring

Three weeks after the start of medication, Peanut was returned for examination, including CBC, chemistry, TT4, urinalysis, and blood pressure measurement. Her weight had stabilized, and night-time vocalizations had declined. Testing revealed a normal CBC, liver values, urine protein:creatinine ratio, and blood pressure, although Peanut had isosthenuric urine and mild azotemia. Reversal of hyperthyroidism may be associated with decreased glomerular filtration rate and a decline in renal function, unmasking the presence of underlying renal disease, which is likely in this case. Most cats have a normal TT4 within 2 to 3 weeks of starting medication3; however, Peanut's condition over-corrected, and she was now slightly hypothyroid at 0.8 µg/dL (reference range, 1-4 µg/dL).1

The patient's dose of FELIMAZOLE Coated Tablets was decreased to 2.5 mg q24h. Both hypothyroidism and hyperthyroidism can be harmful to patients with chronic kidney disease, and hyperthyroidism should not be maintained simply to control azotemia. Patients with concurrent kidney disease should

be treated appropriately based on their IRIS stage.³

Subsequent 3- and 6-week testing showed the patient was euthyroid at $1.5 \, \mu g/dL$, the low end of the reference range on her new dose. Regular rechecks were performed every 3 months. She continued to do well and did not show any other medication-related side effects. Side effects are less common after 2 to 3 months of treatment and have not been shown to be dose-related.³

Conclusion

Treatment in this case improved both Peanut and her owner's quality of life. In these cases, catching disease early helps prevent or delay the onset of comorbidities especially of the eyes, heart, and kidneys.

VALUABLE RESOURCES

- Plumb's Therapeutics Brief:
 Medications that Suppress Thyroid
 Function
- American Association of Feline
 Practitioners Hyperthyroid Guidelines
- Dechra Support Materials for Hyperthyroidism

REFERENCES AND ADDITIONAL MATERIALS

References and additional materials available at **brief.vet/hyperthyroidism**

TABLE

COMPARING TREATMENTS FOR FELINE HYPERTHYROIDISM⁵

Treatment	Pros	Cons
Radioactive iodine (I ¹³¹)	▶ 95% cure rate▶ Treats carcinomas▶ Serious side effects rare	 Referral usually required High initial costs Hospitalization, radioactive material management Irreversible
Methimazole	 95% response rate Most euthryoid in 3 weeks No hospitalization or referral Minimal initial costs Stabilizes for other therapies 	 Does not prevent progression Regular testing required Side effects possible Lifelong treatment required Must assess for underlying conditions prior to therapy
lodine-Restricted Diet	 82% response rate in 1 year No hospitalization, referral, or medication Minimal initial costs 	 Strict diet and treat limitations Does not prevent progression Euthyroidism may take 180 days Lifelong treatment
Thyroidectomy	 90% cure for bilateral surgery (30%-60% unilateral) No specialized equipment 	 Requires general anesthesia Risk of damaging important nearby structures Irreversible Does not address possible mediastinal disease High initial costs

Top 5 Viral **Dermatoses** in Cats

Liora Waldman, BVM&S, CertSAD, MRCVS Veterinary Dermatology & Allergy Center Haifa, Israel

Alexander Werner, VMD, DACVD Animal Dermatology Center Studio City, California



Viral dermatoses in cats are rare diseases caused by direct viral cytopathic effects in the skin. Viral infections are diagnosed using techniques such as PCR, immunohistochemistry, and in situ hybridization. Presented below are the authors' top 5 feline viral dermatoses most likely to be encountered in veterinary practice.

Papillomavirus Papillomavirus influences cell growth and differentiation and may cause cancer.1 Although in general the viruses are species-specific, human and bovine papillomaviruses have been detected in cats.² Four feline papillomaviruses have been completely sequenced. FcaPV-2 is the most frequently isolated from cat lesions^{1,3,4} and was found on the skin of 52% of cats in

one study.5 FcaPV-2 and FdPV-3 are closely related to canine PV-1 and canine PV-7,3 respectively.

Papillomavirus causes the following dermatoses in cats:

▶ **Viral plaques** are uncommon and are seen as single or grouped round-tooval scaly, gray, tan, or black papules or plaques with hyperkeratosis (Figure 1).6 They are neither pruritic nor painful and may be present anywhere on the body. In healthy cats, they may resolve spontaneously.2 In immunosuppressed cats (eg, those with FIV, FIP, FeLV, or neoplasia; those receiving glucocorticoid treatment), resolution occurs after treating the primary cause. Demodex cati mites might be found in the lesions. 1,6-9

TOP 5 VIRAL DERMATOSES IN CATS

- 1. Papillomavirus
- 2. Feline Herpesvirus 1
- 3. Feline Calicivirus
- 4. Feline Pox Virus
- 5. Feline Leukemia Virus

▶ Bowenoid in situ carcinoma (BISC; ie, Bowen's disease) is often a progression from viral plaque. It presents as hyperpigmented macules or crusted plaques that may ulcerate. The face, neck, and limbs are predisposed, but lesions can be seen anywhere on the body.3 Cutaneous horns may be present.¹⁰ BISC can progress to squamous cell carcinoma with metastases.11 Ultraviolet light does not affect neoplastic transformation (Figure 2).2,8,9



▲ FIGURE 2 Ulceration, bleeding, alopecia, and hyperkeratotic plaques on the face of a cat with Bowen's disease caused by papillomavirus infection



▲ FIGURE 3 Twelve-year-old domestic shorthair cat with FHV-1 dermatitis

- ▶ Cutaneous papilloma is rare and appears as a single pedunculated or cauliflower-like hyperkeratotic lesion, smaller than 0.5 cm, at any body site.2,8
- ▶ **Oral papilloma** is also rare. Only 2 cases have been reported, found on the tongue as small, multifocal, soft, pink, raised, flat-topped lesions. 12
- ▶ Feline sarcoid is seen in cats in rural areas and is likely caused by bovine papillomavirus.¹³ Sarcoid lesions are firm, round, single masses that can ulcerate and occur mainly on the nose, upper lip, and digits. They do not metastasize but may recur after excision.8-10
- ▶ Basal cell tumors are uncommon and usually appear as a soft, mobile, painless, dermal mass with some surface scaling. A novel papillomavirus similar to FcaPV-314 has been identified.
- ▶ Papillary squamous cell carcinoma is seen on the head as hornlike crusted masses.6
- ▶ Fibrosarcoma and apocrine gland cysts are rarely associated with papillomavirus.^{2,15}

Diagnosis is made via histopathology, PCR (swab more sensitive than formalin fixed tissue¹), immunohistochemistry, in situ hybridization, or electron microscopy.^{9,10}

Treatment of oral papilloma and single plaques may include excision, cryosurgery, electrosurgery, or CO₂ laser ablation. Some plaques might regress following control of the primary problem. Imiquimod can be effective for plaques and BISC within 3 to 4 weeks. Lesions can recur when treatment is discontinued.^{8,10} Side effects may include local erythema and, occasionally, systemic effects (eg, nausea, vomiting, myalgia, fever, hypotension).¹⁶ Interferon-α (IFNα; 30 units PO q24h) has been reported to be effective.¹⁰

Feline Herpesvirus 1 FHV-1 primarily causes facial dermatitis affecting the nasal planum, muzzle, bridge of nose, and periocular skin (Figure 3), but it can occur at other sites.¹⁷⁻¹⁹ Recent upper respiratory infection, stress, and/or glucocorticoid therapy may precede onset.

Facial lesions may start unilaterally with vesicles, erythema, and alopecia. Due to intense pruritus, lesions may become ulcerated and crusted.

Differential diagnoses include allergy (eg, food, atopy) and eosinophilic plaque. ¹⁹ Diagnosis is made via histopathology, revealing eosinophils, neutrophils or lymphoplasmacytic dermatitis, necrosis, or ulceration with intranuclear inclusion bodies. PCR from fresh biopsy (preferably in saline, not formalin) should be submitted for definitive diagnosis. ^{19,20}

Treatment options include famciclovir (90-125 mg/kg q8-12h^{19,20}), recombinant feline interferon ω (1.5 million units/kg perilesionally and SC for 2-3 weeks) or recombinant feline interferon- α (1 million units/m² SC 3 times per week).²¹ Topical idoxuridine, cidofovir, or trifluridine is used to treat ulcerative keratitis. Vaccination can protect cats from developing lesions.

3

Feline Calicivirus

Feline calicivirus is an RNA virus that is shed via ocular, nasal, and oral secretions. ^{10,22}

Dermatologic signs may include ulcers on the nasal philtrum, lips, tongue, gingiva, and paws¹⁰; swollen feet; facial skin erosions, especially of the nose; and ventral pustules (*Figure 4*).²¹

Differential diagnoses include nasal ulceration (eg, from FHV-1, squamous cell carcinoma, other neoplasia, *Cryptococcus* spp, *Sporothrix schenckii*, or mosquito hypersensitivity), and ulceration of the paws (eg, from pox virus, papillomavirus, FeLV, malignancy, plasma cell pododermatitis).

Treatment with antibiotics might be needed if secondary bacterial infection develops. Oral glucocorticoids may be beneficial to treat oral ulceration.

4

Feline Pox Virus

Feline pox virus dermatitis, caused by cowpox virus, is a rare disease seen primarily in Europe and West Asia. Cats are

infected by hunting rodents (the natural hosts), typically in rural areas. Lesions occur mostly on the head, ears, neck, and legs. Primary lesions may look like bite wounds, nodules, plaques, crusted papules, ulcers, abscesses, or cellulitis (*Figures 5* and 6, next page). Pruritus is variable. Crust-covered, ulcerated papules and nodules typically develop within 1 to 3 weeks. Oral ulceration can lead to anorexia. Fever, conjunctivitis, and pneumonia may develop. 10,23,24



▲ FIGURE 4 Ulceration with crusting on the nose, philtrum, muzzle, and upper lip of a calicivirus-infected cat. Image courtesy of Stephen White, DVM



▲ FIGURE 5 Ulceration on the head and face and crusted ulcer in the medial canthus of the left eye in a cat infected by cowpox virus. *Image courtesy of Tim Nuttall, BVSc, PhD*

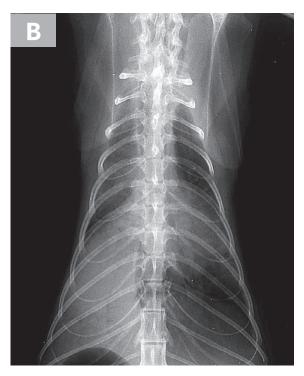
BISC = Bowenoid in situ carcinoma

Pox virus is zoonotic, especially in immunosuppressed humans.

Differential diagnoses include bacterial and fungal infections, neoplasia (mast cell tumor, lymphoma), and granuloma. Diagnosis is made via biopsy (eosinophilic intracytoplasmic inclusion bodies), serology, PCR, immunohistochemistry, or virus isolation.

Most patients recover without complications. Treatment may include antibacterial drugs for secondary





▲ FIGURE 6 Plagues and ulcer on the body of a cat with pox virus (A). The same cat with pneumonia due to pox virus (B). Images courtesy of Tim Nuttall, BVSc, PhD

infections and supportive treatment. Glucocorticoids are contraindicated.

Feline Leukemia Virus FeLV, a retrovirus, causes giant-cell dermatosis^{10,25} with pruritus, ulceration, and crusting lesions—mainly on the head, neck, and face (Figure 7) but occasionally on the extremities or footpads, trunk, and mucocutaneous junctions of the anus and/or prepuce. Cutaneous horns may be seen.¹⁰

Differential diagnoses include evident pruritus caused by allergy (eg, food, atopy), *Notoedres cati*, Cheyletiella spp, or Demodex spp; or crusted lesions caused by exfoliating dermatitis, pemphigus foliaceus, drug reaction, systemic lupus erythematosus, or seborrhea. Diagnosis is made via histopathology (giant-cell dermatoses), serology, or PCR. 10,25,26

See page 93 for references.



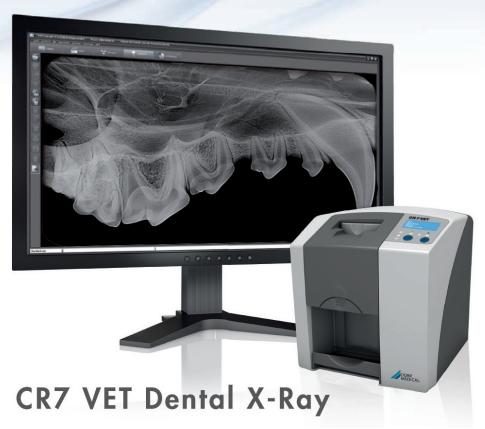
▲ FIGURE 7 Thirteen-year-old FeLV-positive cat with alopecia, mildly seborrheic dermatitis, and excoriations on the ventral

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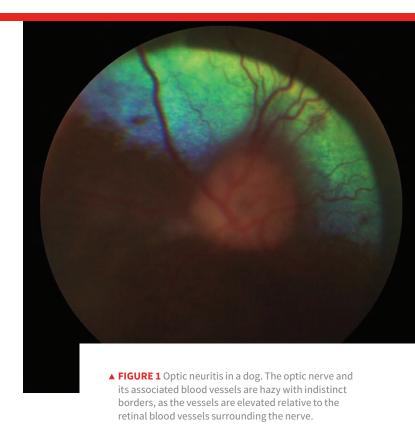
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Optic Neuritis

Anansa Persaud, DVM Long Island Veterinary Specialists Plainview, New York

Thomas Chen, DVM, MS, DACVO University of Tennessee



Optic neuritis is a rare but serious condition that can result in acute blindness or visual deficits in one or both eyes. 1,2 Prompt diagnosis and treatment are necessary to recover vision, and evaluation for neurologic, infectious, and/or neoplastic disease may also be warranted. 1,3,4

Clinical Signs

In cases of bilaterally affected animals, owners often report suspected vision loss based on a clinical history of the pet bumping into walls or objects, missing treats, or having difficulty with stairs. Astute owners of pets with unilateral disease may report more subtle changes (eg, visual deficits, anisocoria with the dilated pupil in the affected eye).

Absent menace responses, with absent pupillary light reflexes and mydriatic pupils, are usually

noted on ophthalmic examination.^{1,5} Further vision testing (eg, visual placement testing, maze) can help confirm lack of vision.

A thorough fundic examination is crucial for including optic neuritis in the list of diagnostic differentials. The optic nerve head most often appears swollen, hyperemic, or elevated (Figure 1). Chorioretinitis with associated focal retinal detachment or edema, hemorrhage, or white or gray foci can also be present adjacent to or near the optic nerve head. Rarely, inflammation can also occur posterior to the optic nerve head (retrobulbar) and therefore cannot be appreciated except with advanced imaging (eg, MRI).5

Diagnosis

Optic neuritis is often diagnosed by confirmation of blindness and pupillary light reflex deficits and visualization of an abnormal optic nerve head on fundic examination. Other important rule outs for blindness can include diffuse retinal detachment

(in contrast to focal detachment proximal to the optic nerve head) and sudden acquired retinal degeneration syndrome. Retinal detachment can also be diagnosed on fundic examination, whereas sudden acquired retinal degeneration syndrome can only be confirmed with an electroretinogram. Performing a complete neurologic examination and obtaining a thorough history are also recommended to assess for concurrent neurologic signs that might be suggestive of meningoencephalitis.

Causes

Optic neuritis in dogs is most often the result of immune-mediated and/or inflammatory brain disease, which together comprise approximately 80% of optic neuritis cases in a study of 96 dogs. Other causes in dogs include infection or neoplasia. Optic neuritis in cats occurs secondary to infectious or neoplastic causes, with no reports of immune-mediated causes or incidence rates for all causes in cats.

Immune-Mediated

Immune-mediated optic neuritis appears to be the most common diagnosis in dogs.^{1,5} The optic nerve is a direct extension of the CNS; therefore, inflammatory brain disease can extend to or focally involve the optic nerves, usually bilaterally. Meningoencephalitis of unknown etiology (MUE; or, when confirmed histologically,

Optic neuritis in dogs is most often the result of immune-mediated and/or inflammatory brain disease, which together comprise approximately 80% of optic neuritis cases in a study of 96 dogs.¹ subtyped more specifically as granulomatous meningoencephalitis [GME]) is one such condition¹⁰ and has been categorized by neurologists as *ocular GME* when inflammation involves the optic nerves, either alone or with concurrent MUE/GME signs.¹¹

In contrast, veterinary ophthalmologists have historically considered optic neuritis (in patients without concurrent neurologic clinical signs) a separate clinical entity from MUE.² A difference in signalment in canine patients with isolated involvement of the optic nerves has been reported; MUE patients were typically female small-breed dogs, whereas isolated optic neuritis patients were often male medium-to-large-breed dogs.¹ The exact relationship or difference between the syndromes, if it exists, has not yet been definitively determined.

Whether a manifestation of MUE or isolated immune-mediated optic neuritis, definitive diagnosis often requires an MRI and CSF tap while also ruling out other infectious or neoplastic diseases; however, many owners often decline advanced imaging or CSF taps due to cost or availability.¹

Infectious Disease

Infectious diseases, with tropism for or involvement of the CNS, have also been reported to cause optic neuritis. Infectious optic neuritis usually manifests as an extension of more generalized or multifocal meningoencephalitis or from ocular and orbital involvement. Fungal disease in particular can involve the orbit or neighboring areas (eg, nasal or sinus cavities) and may result in subsequent involvement and inflammation of the optic nerve.^{1,12} Viral diseases (eg, distemper, tick-borne encephalitis virus, feline infectious peritonitis) affect the nervous tissue directly or indirectly via damage from host immune responses. These diseases can also result in uveitis (both anterior and posterior) or chorioretinitis (not necessarily associated with the optic nerve), the presence of which should raise clinical suspicion of infectious disease as compared with immune-mediated meningoencephalitis.

In dogs, optic neuritis has been reported with distemper virus, tick-borne encephalitis virus, ehrlichiosis, *Toxoplasma gondii* or *Neospora caninum* infections, and fungal disease (eg, aspergillosis, cryptococcosis, histoplasmosis, blastomycosis). ^{1,13-20} In cats, *T gondii* infections, feline infectious peritonitis, and systemic fungal disease (ie, histoplasmosis, cryptoccosis) have been reported with optic neuritis. ^{6-9,17,21}

Infectious disease testing should be conducted based on clinical suspicion from history and signalment (eg, unvaccinated animal, use of tick preventives), geography (for fungal disease), tick exposure, and exploratory bloodwork.

Neoplasia

Primary optic nerve tumors, including optic nerve meningioma and gliomas, have been reported, although they are rare. 1,5,22,23 Orbital neoplasia can also affect the optic nerve. In a case series involving 53 neoplastic cases, carcinomas were seen most commonly (30%), followed by sarcomas (20%), lymphoma (15%), and presumptive meningiomas (17%). 5 Carcinomas and sarcomas were noted to occasionally arise from neighboring areas of the orbit (ie, frontal bone or sinus, nasal cavity, maxilla) that extended into the orbit with involvement of the optic nerve.

Extension of Orbital Disease

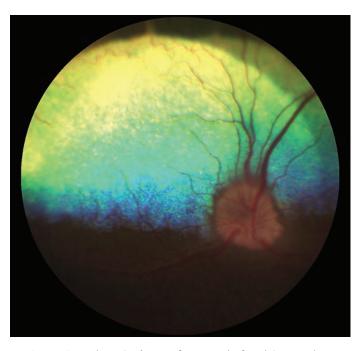
Optic neuritis may also occur secondary to orbital inflammation, including retrobulbar cellulitis and/or abscessation, which can be associated with infection, neoplasia, foreign body, or dental disease. 5,8,19,24-28 If inflammation is severe or near enough to the optic nerve, compression or inflammation of the optic nerve can result in subsequent blindness. Clinically, these conditions can be observed as change in the position or placement of the eye (eg, enophthalmia, exophthalmia), protrusion of the third eyelid, and/or difficulty or pain on opening of the mouth, with periocular swelling and inflammation. Optic neuritis secondary to orbital or retrobulbar inflammation can be unilateral depending on the laterality of the

primary disease (eg, unilateral in bacterial retrobulbar cellulitis).

Treatment & Prognosis

Ultimately, treatment of optic neuritis depends on the underlying cause. Because immune-mediated causes largely predominate, treatment typically involves short-term immunosuppressive doses of steroids (*Figure 2*). Partial or full return of vision was noted in approximately 30.6% (22/72) of dogs in one study¹ and 64% (7/11) of dogs in another.⁴ Return of vision 1 to 2 weeks after initiating therapy for acute blindness has been noted (author experience).

Recurrence has been noted in 2 cases at 15 and 18 months after successful treatment and at 2 weeks after tapering steroids. For optic neuritis that is suspected to be occurring secondary to MUE, treatment recommendations by neurologists generally entail life-long administration of steroids and/or immunomodulatory agents. 11



▲ FIGURE 2 Same dog as in Figure 1 after a month of prednisone and cytarabine treatment. The margins around the optic nerve are still indistinct but much improved. Vessels overlying the nerve can be clearly seen and are in the same plane as the surrounding retinal blood vessels.

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Immunosuppressive doses of steroids can be detrimental if an underlying infection is present and may mask clinical signs or delay diagnosis if an underlying neoplastic disease is present. Any indication of orbital disease should be closely investigated before initiating steroidal treatment. Ideally, infectious disease should be ruled out, with specific testing conducted before initiating steroidal treatment, and an MRI and CSF tap performed to definitively rule in immune-mediated optic neuritis. However, if regaining vision is a priority and immune-mediated disease is suspected, empiric treatment with steroids can be initiated, as long as owners are educated regarding the risks.

Specific treatment for infectious disease or neoplasia will vary depending on the causative or suspected causative agent. Prognosis varies depending on CNS involvement and severity of primary disease but, for vision, is generally considered poor.

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FROM PAGE TO PATIENT

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



- Gabapentin & Fear in Cats
 Karen Lynn C. Sueda, DVM, DACVB
- Screening Obstructed Cats
 Zenithson Ng, DVM, MS, DABVP
 (Canine and Feline Practice)
- Another Tool for Detecting Benign Prostatic Hyperplasia

 Bruce W. Christensen, DVM, MS, DACT
- Intervertebral Disk
 Herniation: In-House
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Gabapentin & Fear in Cats

Karen Lynn C. Sueda, DVM, DACVB VCA West Los Angeles Animal Hospital

Los Angeles, California

In the Literature

Pankratz KE, Ferris KK, Griffith EH, Sherman BL. Use of single-dose oral gabapentin to attenuate fear responses in cage-trap confined community cats: a double-blind, placebo-controlled field trial. *J Feline Med Surg*. 2017. doi:10.1177/1098612X17719399

FROM THE PAGE ...

Trap-neuter-return programs are used extensively for population control among unowned community cats. During trapping and perioperative cage confinement, cats may experience high levels of stress and self-inflicted trauma. Gabapentin, an anticonvulsant used in the treatment of neuropathic pain, has been shown to reduce anxiety in rats and humans. Although gabapentin's anxiolytic properties have not been studied in cats, pharmacokinetics studies have reported excellent oral bioavailability and a wide margin of safety with single-dose administration.

In a double-blind, placebo-controlled study, the behavior of 53 unowned community cats estimated to be older than 4 months were individually cage trapped, confined, and observed during a regional trap-neuter-return program. Following baseline behavior observation, cats were randomly assigned to receive one of 3 oral suspension treatments: low-dose gabapentin (50 mg/cat), high-dose gabapentin (100 mg/cat), or placebo. During baseline and 1, 2, 3, and 12 hours posttreatment, each cat's stress score, global sedation score, and respiratory rate were determined. Additionally, a facial injury score was assigned at baseline, 12 hours posttreatment, and during sterilization surgery. After 12 hours, cats were anesthetized and underwent sterilization.

Gabapentin doses ranged from 9.2-47.6 mg/kg. Cats receiving either low- or high-dose gabapentin had significantly lower stress scores 2 and 3 hours posttreatment as compared with controls. There were no significant differences between low- and high-dose group stress scores at any time. All 3 groups exhibited a decline in respiratory rate over the 3 hours after treatment. No significant differences in sedation scores were observed

for any group at any time. Facial injuries were observed in all groups and did not vary over time. No adverse events attributable to gabapentin were noted; all cats successfully and uneventfully underwent anesthesia and sterilization surgery. Hypersalivation was observed in 4 cats (placebo, 2; low-dose, 1; high-dose, 1).

... TO YOUR PATIENTS

Key pearls to put into practice:

- In cats, single-dose gabapentin (50-100 mg/cat) may result in decreased stress, but not necessarily sedation, 2 to 3 hours after oral administration.
- Gabapentin may be safely administered before anesthesia and routine surgery in healthy patients older than 4 months.
- Oral administration of a liquid suspension of gabapentin is generally well tolerated, although hypersalivation may occur in some patients.

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Suggested Reading

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Reference: 1. Nobivac[®] Canine Flu Bivalent [product label]. Madison, NJ: Merck Animal Health.





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Screening Obstructed Cats

Zenithson Ng, DVM, MS, DABVP (Canine and Feline Practice) *University of Tennessee*

In the Literature

Neri AM, de Araújo Machado LH, Guimarães Okamoto PT, et al. Routine screening examinations in attendance of cats with obstructive lower urinary tract disease. *Top Companion Anim Med.* 2016;31(4):140-145.

FROM THE PAGE ...

Feline obstructive lower urinary tract disease (FLUTD) diagnosis is based on history of stranguria, palpation of a firm distended bladder, and presence of ischuria. Metabolic and hemodynamic abnormalities often result and should be documented before anesthesia is administered for unobstruction. This study described a standardized diagnostic protocol and results from 26 male cats that were presented for urethral obstruction.

In addition to history and physical examination, a minimum database (ie, blood pressure measurement, ECG, serum chemistry profile, blood gas analysis) was collected. Urine for urinalysis was collected from 17 cats via cystocentesis. Despite concerns regarding cystocentesis in obstructed cats, no adverse effects were reported.

Cats that were obstructed for more than 36 hours had greater hemodynamic and metabolic abnormalities than did cats obstructed for less than 36 hours. Arrhythmias were noted in 15.38% of cats with a serum potassium greater than 8.5 mEq/L; a previous study found arrhythmias were not correlated directly with the magnitude of electrolyte abnormalities. Despite hyperkalemia being a common finding in this population, bradycardia was infrequent (7.69% of cats). The authors proposed that sympathetic activation from stress and pain may have masked bradycardia, which would have typically been present.

Most cats (69.24%) were normotensive, but ionized calcium levels were significantly lower in normotensive cats as compared with hypertensive cats. This is concerning because calcium concentration has been shown to be lower in nonsurvivors as compared with survivors.³ Therefore, it cannot be assumed that normotensive patients are

metabolically stable, as these cats had more significant laboratory changes as compared with hypertensive cats. Less than half of these cats (46.15%) were able to be unobstructed via urethral catheterization; the remaining cats (53.85%) were surgically unobstructed via perineal urethrostomy.

This proposed protocol of clinical screening examinations during early treatment of obstructed cats provides a dynamic assessment that can be monitored continually as therapy is instituted.

... TO YOUR PATIENTS

Key pearls to put into practice:

- Prepare owners by communicating clearly that failure to correct obstruction via urethral catheterization is common and warrants surgical intervention.
- Normal heart rate and blood pressure do not rule out laboratory abnormalities.
 Electrolytes should be measured in all patients, even for normotensive patients and in the absence of bradycardia.
- Hypothermia is a common clinical finding and may reflect the magnitude of urinary obstruction and associated clinicopathologic abnormalities.

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Another Tool for Detecting Benign Prostatic Hyperplasia

Bruce W. Christensen, DVM, MS, DACT University of California, Davis

In the Literature

Pinheiro D, Machado J, Viegas C, et al. Evaluation of biomarker canine-prostate specific arginine esterase (CPSE) for the diagnosis of benign prostatic hyperplasia. *BMC Vet Res.* 2017;13:76. doi:10.1186/s12917-017-0996-5

FROM THE PAGE ...

Nearly all intact male dogs eventually develop benign prostatic hyperplasia (BPH). Although most will show no clinical signs and therefore will not require treatment, some may exhibit hemospermia, hematuria, tenesmus, dysuria, prostatomegaly, poor semen quality, infertility, and serosanguinous urethral discharge not associated with urination. Diagnosis of prostatic disorders typically relies on clinical history, physical examination (including digital rectal examination), ultrasonography, and prostatic cytology. Use of canine prostate-specific arginine esterase (CPSE) as a biomarker that can reliably and specifically increase with the development of BPH in dogs has been promoted.

In this study, 60 intact dogs were divided into 2 groups (BPH [n=29]; median age, 9 years] and nonBPH [n=31]; median age, 5 years]) based on prostatic cytology obtained from fine-needle aspiration or prostatic massage. Clinical history, physical examination, ultrasonographic evaluation, and CPSE values were all recorded. Differences between CPSE concentrations in BPH and nonBPH groups were compared, and correlations between CPSE and other variables were measured. A significant difference in median CPSE levels was detected between BPH and nonBPH groups. Significant positive correlations were detected between mean CPSE levels and age or prostatic volume, as well as clinical examination findings, ultrasonographic findings, and positive cytology results. The high sensitivity of CPSE demonstrated in this study justifies the addition of this assay to the list of tools for the diagnosis of canine BPH. The specificity, however, was lower, with roughly 10% of false-positive results.

... TO YOUR PATIENTS

Key pearls to put into practice:

- A strong correlation between elevated CPSE concentrations and all 3 traditional diagnostic procedures (ie, clinical examination, ultrasonographic evaluation, cytology) suggests that, as with most other medical investigations, definitive diagnoses are most confidently made when incorporating and noting agreement among multiple diagnostic approaches.
- Cytology remains the gold standard for diagnosis of any prostatic disorder. Cytology can be best and—in most cases—easily obtained through manual stimulation of ejaculation, with separation of the prostatic (ie, third) fraction. In cases in which this method is not possible, prostatic massage or ultrasound-guided fine-needle aspiration may be employed.
- CPSE is a sensitive test for canine BPH and can be used as an adjunctive diagnostic test if clinical examination and ultrasonographic evaluation are inconclusive, if diagnostic prostatic cytology cannot be obtained, and/or if quantitative pre- and posttreatment evaluations are desired.

Suggested Reading

Lévy X, Niżański W, von Heimendahl A, Mimouni P. Diagnosis of common prostatic conditions in dogs: an update. Reprod Domest Anim. 2014;49(Suppl 2):50-57.

Smith J. Canine prostatic disease: a review of anatomy, pathology, diagnosis, and treatment. *Theriogenology*. 2008;70(3):375-383.







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Intervertebral Disk Herniation: In-House Postoperative Rehabilitation

Jason Bleedorn, DVM, DACVS
University of Wisconsin–Madison

In the Literature

Hodgson MM, Bevan JM, Evans RB, Johnson TI. Influence of in-house rehabilitation on the postoperative outcome of dogs with intervertebral disk herniation. *Vet Surg.* 2017;46(4):566-573.

FROM THE PAGE ...

In dogs, intervertebral disk herniation (IVDH) is a common and disabling condition that, in severe cases, often requires surgical decompression. Postoperative rehabilitation is often recommended and employed to facilitate a safe and efficient functional recovery; however, despite its widespread popularity and availability, few outcome data exist regarding dogs.

This retrospective study compared clinical outcomes and complications using in-house rehabilitation in dogs (n = 87) following surgical decompression for single-site IVDH. Rehabilitation commenced at a median of 2 weeks postoperatively and consisted of treadmill (land/underwater), laser, and active and passive manual therapies collectively for a median of 12 days and 49 treatments. A control group (n = 161) received laser therapy, passive range-of-motion exercises, and cryotherapy during the immediate postoperative hospitalization period only. At minimum, dogs were examined daily while hospitalized, 10 to 14 days postoperatively, and 4 to 6 weeks postoperatively.

Preoperative neurologic scores were similar between groups. More dogs returned to full neurologic function with rehabilitation (33%) as compared with control dogs (9%). However, mean time to ambulation was faster in control dogs (14 days) as compared with rehabilitation dogs (28 days). Dogs without deep pain were analyzed separately, and outcomes were similar. The complication rate was higher in control dogs (29%) as compared with rehabilitation dogs (16%) and included surgery for recurrent disk extrusion in 3 control cases and one rehabilitation case.

Study results were somewhat difficult to decipher. Dogs with a consistent rehabilitation program experienced a greater return to normal function and fewer complications. In-house rehabilitation allows for frequent examination by rehabilitation specialists and veterinarians to guide an individualized plan and to identify and manage complications. Greater gains would be anticipated, as other studies in human and veterinary medicine have demonstrated. Time to ambulation was prolonged with rehabilitation, likely because of the retrospective study design and inconsistent follow-up in these cases.

... TO YOUR PATIENTS

Key pearls to put into practice:

Early diagnosis and intervention in dogs with IVDH are critical. Surgical decompression should be considered in severe cases, especially for nonambulatory patients.

Prognosis for return to function following surgery is greater than 85% with deep pain perception and approximately 50% without pain.^{1,2}

Communication between veterinarians and rehabilitation specialists is important for development of a rehabilitation plan based on individualized patient assessment and goals.

Multimodal rehabilitation strategies may be beneficial and may include active standing exercises, weight-shifting, and proprioceptive activities and, when appropriate, passive joint mobility, cold laser, and treadmill walking.

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Research Note:

Canine Vision & Color Blindness

To test the hypothesis that canine vision is dichromatic in nature and resembles that of human red–green color blindness, researchers used a modified version of a human color blindness test (Ishihara test) to evaluate an orienting response (ie, movements of the eyes, head, and body) to movements of a colored target in the dog's visual field. Results of this study support the hypothesis, providing a direct comparison with color vision in humans and potentially opening the door for the development of new techniques to assess color vision in animals.

Source

Siniscalchi M, d'Ingeo S, Fornelli S, Quaranta A. Are dogs red-green colour blind? *R Soc Open Sci.* 2017. doi:10.1098/rsos.170869

Research Note:

Palmitoylethanolamide & Homeostasis

Palmitoylethanolamide (PEA) is a bioactive lipid involved in maintaining and restoring cellular homeostasis. The effect of ultramicronized PEA (PEA-um) on mast cells was measured in an ex vivo skin model of canine atopic dermatitis. Cultured skin biopsy samples were treated with either 10 $\mu g/mL$ or 100 $\mu g/mL$ of compound 48/80 (ie, a secretagogue that causes mast cell degranulation), with or without 30 μ M PEA-um. Exposure to PEA-um before and during a 72-hour treatment period with 10 $\mu g/mL$ or 100 $\mu g/mL$ of compound 48/80 caused a marked-to-significant decrease in degranulating mast cells, histamine content, and vasodilation.

Source

 $Abramo\ F, Lazzarini\ G, Pirone\ A, et\ al.\ Ultramicronized\ palmitoyle than olamide\ counteracts\ the\ effects\ of\ compound\ 48/80\ in\ a\ canine\ skin\ organ\ culture\ model.\ \textit{Vet\ Dermatol}.\ 2017;28(5):456-e104.$

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WARNINGS: Methimazole has anti-vitamin K activity and may induce bleeding diathesis without evidence of thrombocytopenia.

HUMAN WARNINGS: Not for use in humans. Keep out of reach of children. Methimazole is a human teratogen. Wash hands with soap and water after administration of methimazole or contact with the litter of treated cats. Do not break or crush tablets. Wear protective gloves to prevent direct contact with litter, feces, urine, or vomit of treated cats, and broken or moistened tablets. Methimazole may cause vomiting, gastric distress, headache, fever, arthralgia, pruritus, and pancytopenia. In the event of accidental ingestion/overdose, seek medical advice immediately and show the product label to the physician.

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CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian As with all drugs, side effects may occur. The most commonly reported side effects are anorexia, vomiting, head/facial pruritus or edema, depression/lethargy, weight loss, anemia, elevated liver enzymes, skin lesions, elevated BUN, diarrhea, and thrombocytopenia. FELIMAZOLE Coated Tablets are not for use in pregnant or lactating queens, or cats with renal, hepatic, or hematological disorders. In some reported cases, the patients recovered after adverse signs were recognized, the drug was withdrawn, and veterinary care was applied. In some cases, death (or euthanasia) has been reported as an outcome of the adverse reactions listed above. Methimazole has anti-vitamin K activity and may induce bleeding diathesis without evidence of thrombocytopenia. Refer to the prescribing information for complete details or visit www.dechra-us.com

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Venous Access in Dogs with Cardiovascular Collapse

Marie K. Holowaychuk, DVM, DACVECC Critical Care Vet Consulting Calgary, Alberta, Canada

In the Literature

Allukian AR, Abelson AL, Babyak J, Rozanski EA. Comparison of time to obtain intraosseous versus jugular venous catheterization on canine cadavers. *J Vet Emerg Crit Care*. 2017;27(5):506-511.

FROM THE PAGE ...

Obtaining IV access can be difficult in veterinary patients with cardiovascular collapse or after cardiopulmonary arrest. In such situations, rapid IV access is imperative to facilitate administration of IV fluids and cardiopulmonary resuscitation medications.

This study compared 2 methods of obtaining rapid vascular access in dogs: intraosseous (IO) catheterization of the humerus via an automatic rotary insertion device and IV catheterization via a jugular venous cutdown. Canine cadavers were used as a model for cardio-pulmonary arrest; cadavers were placed in lateral recumbency in the emergency room, with all necessary materials in their normal locations, to simulate a hospital CPR setting. An assistant was available to hold off the vein or stabilize the leg for catheterization.

Four categories of catheter placers participated in the study: a veterinary technician specialist certified in emergency medicine, an experienced emergency and critical care specialist, a first-year emergency and critical care resident, and a final-year veterinary student on the emergency and critical care rotation. Verbal instructions on how to perform jugular venous cutdown and place an IO catheter were given. Catheter placement was timed, and fluoroscopy was used to confirm proper placement once complete.

Cadaver body weight ranged from 13.67 lb to 88.18 lb (6.2-40 kg), and median BCS was 5/9. IO catheterization was faster (median, 55.4 seconds) than IV catheterization (median, 217.3 seconds) for all catheter placers. There was no difference in time among catheter placers for IO catheterization; however, time to achieve IV catheterization varied among



FIGURE An IO catheter is inserted into the humerus of a canine cadaver using an automatic rotary insertion device. Image courtesy of Marie K. Holowaychuk, DVM, DACVECC

catheter placers (range, 55.6-614 seconds). The overall success rate for both types of catheter placements was 87.5%.

... TO YOUR PATIENTS

Key pearls to put into practice:

- Venous access can be achieved faster using IO catheterization with an automatic rotary insertion device as compared with IV catheterization of the jugular vein in dogs with cardiovascular collapse.
- 2 IO catheterization time is not affected by catheter placer experience, whereas jugular catheterization using venous cutdown requires practice and is performed more quickly by experienced personnel.
- IO catheterization using an automatic rotary insertion device does not require an incision and enters the medullary cavity of the bone, where vascular collapse does not occur.
- The selected IO catheter length must be sufficient to reach the medullary cavity to ensure successful placement.

IV Fluid Bag Contamination

Amanda A. Cavanagh, DVM, DACVECC Colorado State University

In the Literature

Guillaumin J, Olp NM, Magnusson KD, Butler AL, Daniels JB. Influence of hang time and location on bacterial contamination of intravenous bags in a veterinary emergency and critical care setting. *J Vet Emerg Crit Care*. 2017;27(5):548-554.

FROM THE PAGE ...

To avoid fluid contamination and subsequent bloodstream infection in humans, the Centers for Disease Control and Prevention recommends discarding IV fluids within 24 hours of initial use. However, these guidelines were developed when glass IV fluid bottles were more likely to become contaminated during manufacturing due to poor quality control. No updated guidelines for hospitalized humans have been published, nor have veterinary guidelines been published.

The purpose of this study was to determine the bacterial contamination rate of IV fluid bags and their fluid while hanging in the veterinary emergency room or intensive care unit. This experimental study mimicked a clinical environment in which IV fluid bags were punctured multiple times during reutilization. IV fluid bags were hung near sinks and open supply bins in the emergency room and intensive care unit for 11 days (ie, days 0-10). Each day, the bags were punctured 3 times with sterile needles; of note, the study design purposefully called for not disinfecting the injection port. The investigators then cultured the bags' access ports and fluid on days 0, 2, 4, 7, and 10. By day 7, 31.1% of access ports and 4.4% of fluids were contaminated. Port contamination was more likely if bags were located near a sink. No fluids were contaminated on days 0 or 2, which indicated that fluid contamination occurred between days 2 and 4.

IV fluids will support bacterial growth if contaminant bacteria are introduced to the bag, which puts patients at risk for bloodstream infections.²

... TO YOUR PATIENTS

Key pearls to put into practice:

- Swabbing access ports with a salinesoaked cotton swab mechanically removes greater than 99% of microorganisms; using 70% ethanol increases microbe eradication.³
- IV fluid bags should not be used as a source of saline flush solutions because of the risk for contamination. Commercially available prefilled saline syringes can decrease the risk for bacterial contamination and subsequent catheter-related bloodstream infection.⁴
 - Fluid administration sets should be replaced every 4 to 7 days. 5 Administration sets used to deliver blood products or parenteral nutrition should be replaced every 24 hours. 6 There are no recommendations for the frequency of fluid bag replacement, but bags should at least be replaced with each administration set change. The same fluid bag should not be used in more than one patient. 6

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Electrosurgery vs Cold Instruments in Midline Abdominal Incisions

Kristy Broaddus, DVM, MS, DACVS

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In the Literature

Meakin LB, Murrell JC, Doran ICP, et al. Electrosurgery reduces blood loss and immediate postoperative inflammation compared to cold instruments for midline celiotomy in dogs: a randomized controlled trial. *Vet Surg.* 2017;46(4):515-519.

FROM THE PAGE ...

Concerns that healing after electrocautery is inferior as compared with healing after sharp dissection with cold instruments have been reported. Historically, a rodent model showed reduced tensile strength in abdominal incision healing with electrocautery use.\(^1\) However, in most wound healing models, electrocautery has been used in coagulation mode, which is more destructive than lower voltage cutting mode. In addition, due to species differences, a direct correlation cannot be proven from rodents to dogs without direct examination.



▲ FIGURE 1 Use of a polar instrument to create a parapatellar incision (ie, cutting mode) and to pinpoint individual vessels (ie, coagulation mode)



▲ FIGURE 2 Use of a bipolar instrument for delicate tissue dissection and individual vessel coagulation. Bipolar has only one mode.

Continues ▶

This study examined routine sharp excision with scalpel blade and scissors versus electrocautery in cutting mode to create a midline abdominal incision from skin through the linea alba in 120 dogs. Dogs were evaluated in hospital at 24 and 48 hours postoperation for pain and incisional complications. Wound healing was found to be similar, with reduced blood loss documented in the electrosurgery group. Electrocautery was associated with significantly less incision redness at 24 hours postoperation as compared with cold instrument technique. Both groups were similar thereafter.

Although more precise evaluation of wound healing and followup would have been beneficial, this study can be helpful in providing assurance regarding the safe use of electrosurgery in routine abdominal incisions. This information is especially useful for anemic or coagulopathic patients, in which blood conservation is paramount. Caution should always be taken with the use of cautery to avoid excessive tissue damage. Pairing electrosurgery alongside traditional cold instruments likely leads to an optimal solution, maximizing the benefits of both techniques.

... TO YOUR PATIENTS

Key pearls to put into practice:

Electrosurgery can be monopolar or bipolar. Monopolar requires a grounding source, typically a ground plate placed under the patient. A grounding plate must be adequately placed to avoid serious cautery burns. The bipolar type is self-grounding through the forceps tips and is typically more precise. Tips must be 1 mm apart to work appropriately.

Monopolar cautery has 2 modes: cutting and coagulation. Electrocautery in cutting mode is best for focal tissue dissection, whereas coagulation mode is best for individual bleeding vessels. Monopolar cautery requires a relatively dry field, whereas bipolar tolerates more fluid.

The use of traditional cold instruments, along with varying amounts of electrocautery, is likely beneficial to most surgical patients. Sharp skin and linea alba incisions can be paired with electrocautery in the subcutaneous region to achieve the benefits of both techniques.

Reference

Kumagai SG, Rosales RF, Hunter GC, et al. Effects of electrocautery on midline laparotomy wound infection. Am J Surg. 1991;162(6):620-622.



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

Description:

NexGard* (afroxolaner) is available in four sizes of beef-flavored, soft chewables for oral administration to dogs and puppies according to their weight. Each chewable is formulated to provide a minimum afroxolaner dosage of 1.14 mg/lb (2.5 mg/kg). Afroxolaner has the chemical composition 1-Naphthalenecarboxamide, 4-[5-13-chloro-5-(trifluoromethyl)-phenyl]-4, 5-dihydro-5-(trifluoromethyl)-3-isoxazolyl]-N-{2-oxo-2-{12.2,2-trifluoromethyl}-aminolethyl.

Indications:

NexGard kills adult fleas and is indicated for the treatment and prevention of flea infestations (Ctenocephalides felis), and rescusar and adult measures and is indicated in the remainer and pelvention on their indexions (claimed and in the reatment and control of Black-legged tick (treatment and control of Black-legged tick (treatment), American Dog tick (Demacantor variabilis). Lowe Start tick (Amblyomma americanum), and Brown dog tick (Phipicephalus sanguineus) infestations in dogs and pupples 8 weeks of age and older, veighting 4 pounds of body weight or greater, for one month.

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

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

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

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

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

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

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

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

Precautions:
The safe use of NexGard in breeding, pregnant or lactating dogs has not been evaluated. Use with caution in dogs with a history of seizures (see Adverse Reactions).

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

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

Table 1: Dogs With Adverse Reactions

III AUVEISE HEACHORS.	Treatment Group			
	Afoxolaner		Oral active control	
	N¹	% (n=415)	N ²	% (n=200)
Vomiting (with and without blood)	17	4.1	25	12.5
Dry/Flaky Skin	13	3.1	2	1.0
Diarrhea (with and without blood)	13	3.1	7	3.5
Lethargy	7	1.7	4	2.0
Anorexia	5	1.2	9	4.5

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

In the US field study, one dog with a history of seizures experienced a seizure on the same day after receiving the first dose and on the same day after receiving the second dose of NexGard. This dog experienced at 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 on seizures throughout the study.

To report suspected adverse events, for technical assistance or to obtain a copy of the MSDS, contact Merial at 1-888-637-4251 or www.merial.com/NexGard. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at https://www.fda.gov/AnimalVeterinary/SafetyHealth.

Mode of Action:

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

Effectiveness:

a well-controlled laboratory study. NexGard began to kill fleas four hours after initial administration and demonstrated >99% in a well-controller administration and only all of the well-controlled laboratory study. NexGard demonstrated 100% effectiveness against adult fleas 24 hours post-infestation for 35 days, and was ≥ 93% effective at 12 hours post-infestation for 35 days, and was ≥ 93% effective at 12 hours post-infestation through Day 21, and on Day 35. Do Day 28, NexGard was 811 % effective 12 hours post-infestation. Dogs in both the treated and control groups that were infested with fleas on Day-1 generated flea eggs at 12- and 24-hours post-treatment (0-11 eggs and 1-17 eggs in the NexGard treated dogs, and 490 eggs and 0-118 eggs in the control dogs, at 12- and 24-hours, respectively. At subsequent evaluations post-infestation, fleas from dogs in the treated group were essentially unable to produce any eggs (0-1 eggs) while fleas from dogs in the control group continued to produce eggs (1-141 eggs).

In a 90-day US field study conducted in households with existing flea infestations of varying severity, the effectiveness of NexGard against fleas on the Day 30, 60 and 90 visits compared with baseline was 98.0%, 99.7%, and 99.9%, respectively. Collectively, the data from the three studies (two laboratory and one field) demonstrate that NexGard kills fleas before they can lay eggs, thus preventing subsequent flea infestations after the start of treatment of existing flea infestations. In well-controlled laboratory studies, NexGard demonstrated >97% effectiveness against Demacentor variability. >94% effectiveness against Lowers capapulars, and >93% effectiveness against Thipscaphulas sanguines. A Bhours post-infestation for 30 days. At 72 hours post-infestation, NexGard demonstrated >97% effectiveness against Amblyomma americanum for 30 days.

30 days. At 72 hours post-inlestauun, revaearu usinassaudus and 18 days. Animal Safety:
In a margin of safety study, NexGard was administered orally to 8 to 9-week-old Beagle pupples at 1, 3, and 5 times the maximum exposure dose (6 3 mg/kg) for three treatments every 28 days, followed by three treatments every 14 days, for a total of six treatments. Dogs in the control group were sham-dosed. There were no clinically-relevant effects related to treatment on physical examination, body weight, tood consumption, clinical pathology clinical chemistries, or coagulation tests), gross pathology, histopathology or organ weights. Vomiting occurred throughout the study, with a similar incidence in the treated and control groups, including one dog in the 5x group that vomited four hours after treatment. In a well-controlled field study, NexGard was used concomitantly with other medications, such as vaccines, anthelimitics, In a well-controlled field study, NexGard was used concomitantly with other medications, such as vaccines, anthelimitics, antibiotics (including topicals), steroids, NSAIDS, anesthetics, and antihistamines. No adverse reactions were observed from the concomitant use of NexGard with other medications.

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

How Supplied:

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

NADA 141-406, Approved by FDA

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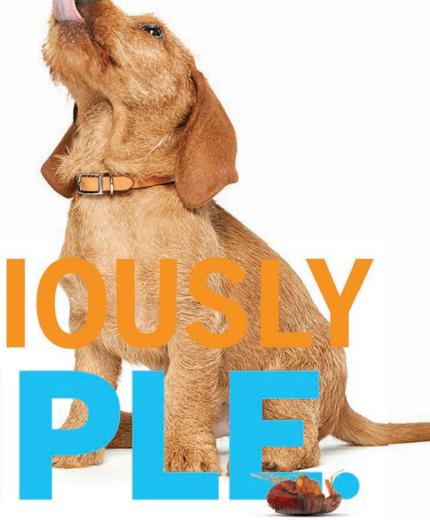
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¹Data on file at Merial. ²Data on file at Merial. Based on veterinary dispensed dose data.

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



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IMPORTANT SAFETY INFORMATION: NexGard® (afoxolaner) is for use in dogs only. The most frequently reported adverse reactions included pruritus, vomiting, dry/flaky skin, diarrhea, lethargy, 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. For more information, see full prescribing information or visit www.NexGardForDogs.com.



Do Backyard Chickens Pose Any Health Risks to Humans?

Casey Barton Behravesh, MS, DVM, DrPH, DACVPM Centers for Disease Control and Prevention Atlanta, Georgia



Owners of backyard chickens and other poultry (eg, ducks, geese, turkeys) should be made aware of the risks these pets pose to humans and take basic biosecurity steps to protect against zoonotic disease transmission. Backyard poultry can appear healthy and clean but can carry *Salmonella* spp or *Campylobacter* spp.¹⁻³ Eggs and habitats can also become contaminated.¹⁻³

Zoonotic diseases that backyard poultry may spread to humans include salmonellosis, campylobacteriosis, and avian influenza viruses. Since the 1990s, numerous widespread outbreaks of human *Salmonella* spp infections linked to contact with backyard chickens have been documented in the United States. Some humans—including children younger than 5 years, humans with weakened immune systems, humans 65 years of age or older, and pregnant women—are at higher risk for serious illness from poultry-borne zoonotic diseases.

Salmonellosis & Campylobacteriosis

Symptoms of salmonellosis or campylobacteriosis include diarrhea (which may be bloody), fever, and/or abdominal cramps. In cases of severe infection, hospitalization may be required and infection may spread from the intestines to the bloodstream and other body sites, which can be life threatening. Infection generally lasts up to one week.

Avian Influenza Viruses

Avian influenza viruses (ie, diseases caused by infection with avian influenza Type-A viruses) occur naturally among wild aquatic birds worldwide and can easily spread and infect domestic poultry and other avian and animal species.⁵ Wild aquatic birds (eg, ducks, geese) can be infected with avian influenza viruses but appear healthy; however, some of these viruses can cause serious illness and death in domestic poultry (eg, chickens, ducks, turkeys). Infected birds can carry viruses in saliva, mucus, and feces.⁵

Avian influenza viruses can infect humans via inhalation or contact with the eyes, nose, or mouth.5 Avian influenza in humans has ranged from mild to severe. Signs and symptoms include fever, cough, sore throat, runny or stuffy nose, muscle or body aches, fatigue, headaches, conjunctivitis, diarrhea, nausea, vomiting, and difficulty breathing. Humans in close or prolonged unprotected contact with infected birds or contaminated environments are thought to be at greater risk for infection, and some humans—including children younger than 5 years, humans with weakened immune systems, humans 65 years of age or older, and pregnant women—are at greater risk for serious illness from avian influenza virus infections. Most

reported avian influenza infections in humans have occurred after unprotected contact with infected birds or contaminated surfaces.⁶

Prevention

Veterinarians should advise owners of backyard chickens and/or other poultry about zoonotic risks and how to reduce the risk for disease transmission:

- Hands should always be washed thoroughly with soap immediately after touching poultry or anything in their habitat.
- Adults should supervise handwashing by young children.
- Hand sanitizer should be used if soap and/or water are unavailable.
- Poultry should not be allowed to enter homes, especially areas where food or drinks are prepared, served, or stored.
- Owners should designate a pair of shoes to wear while caring for poultry and avoid bringing those shoes into the home.
- Children younger than 5 years, those with weakened immune systems, pregnant women, and adults 65 years or older should not handle or touch chicks, ducklings, or other live poultry.
- ► Food or drink should not be consumed in areas where poultry live or roam.
- Birds and other poultry should never be kissed or snuggled, and touching of the face or mouth after handling birds

- should be avoided until hands can be
- ► Equipment or materials used to raise or care for live poultry (eg, cages, feed or water containers) should be cleaned outside the home.

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Suggested Reading

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Updated June 29, 2017. Accessed December
7. 2017.

Zoonotic diseases that backyard poultry may spread to humans include salmonellosis, campylobacteriosis, and avian influenza viruses.



Nutritional Management in a Senior Cat with Weight Loss

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Diet in Disease is a series developed by the WSAVA, the Academy of Veterinary Nutrition Technicians, and Clinician's Brief.



Gregg K. Takashima, DVM

WSAVA Global Nutrition Committee Series Editor

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Academy of Veterinary Nutrition Technicians

THE CASE

A 14-year-old neutered male British Burmese cat (Figure) was presented for a routine geriatric examination. Although he had a good appetite, his weight had decreased from 10.1 lb (4.6 kg) to 9.1 lb (4.14 kg) over the past year.

History

The owner reported that the cat had become less active over the past year, had been sleeping on the floor instead of the couch as he had previously preferred, and may have been urinating increased volumes.



▲ FIGURE The patient showing muscle and weight loss

The patient's diet comprised a combination of commercial adult maintenance dry cat food fed ad libitum and canned cat food fed at approximately 1.8 oz (≈50 g) per feeding twice a day. He had outdoor access only to a fenced garden; to the owner's knowledge, the cat neither hunted nor scavenged. His appetite was good and unchanged over the past year.

The household included another cat, which was fed from a separate bowl; however, the cats often finished one another's food, so the exact amount the presenting cat ate could not be determined.

Physical Examination

The cat's muscle condition score had not been evaluated or recorded the previous year, but

TABLE

SERUM CHEMISTRY RESULTS

Test	Result	Reference Range
Blood urea nitrogen	34.2 mg/dL (12.2 mmol/L)	8.1-27.4 mg/dL (2.9-9.8 mmol/L)
Creatinine	1.57 mg/dL (139 µmol/L)	0.45-2.0 mg/dL (40-177 μmol/L)
Glucose	178 mg/dL (9.86 mmol/L)	71-159 mg/dL (3.94-8.83 mmol/L)
Fructosamine	201 μmol/L	159-295 μmol/L
Total T4	2.95 µg/dL (38 nmol/L)	1.48-5.05 µg/dL (19-65 nmol/L)
SDMA	27.4 μg/dL (1.37 μmol/L)	0-21.4 μg/dL (0-1.07 μmol/L)

mild-to-moderate muscle mass loss is currently evident. BCS, which was 7/9 the previous year, was 6/9 on examination. BCS is an estimate that was designed with healthy adult cats; elderly or ill cats may lose muscle mass (ie, sarcopenia) and retain fat (eg, inguinal fat pads) and therefore are more difficult to score accurately.

The patient was bright and alert, with normal mucous membranes, thoracic auscultation, and abdominal palpation. Respiratory rate was 28 breaths per minute, and heart rate was 180 bpm with synchronous pulses. Blood pressure was 140 mm Hg. Rectal temperature was 100.6°F (38.1°C). He had decreased mobility because of previously diagnosed arthritis in both elbows; some joint thickening was noted, but no crepitus was observed.

Diagnostic Results

Hematology results were within reference ranges.

Urine specific gravity was 1.029; dipstick results were negative for all parameters. Urine culture results were negative. Urine protein:creatinine ratio was 0.18 (reference range, <0.2). Abnormalities in the serum chemistry profile included elevated blood urea nitrogen and elevated glucose without glucosuria (Table). Fructosamine levels were within reference range.

Elevated serum glucose without glucosuria and fructosamine within the reference range is likely a transient rise from stress. Because British Burmese are at risk for diabetes mellitus, fructosamine evaluation was possibly justified, although the glucose value is not consistent with polyuria and/or polydipsia resulting from diabetes mellitus.

The patient's mild azotemia was likely due to prerenal causes (eg, subclinical dehydration), early kidney disease, or both.

DIAGNOSIS:

CHRONIC KIDNEY DISEASE & PRESUMPTIVE OSTEOARTHRITIS

In addition to osteoarthritis, the patient was diagnosed with International Renal Interest Society (IRIS) Stage 1, nonproteinuric, normotensive chronic kidney disease (CKD).¹

Cats with early-stage CKD may be able to concentrate urine more than a dog at the same stage; therefore, the cat's urine specific gravity did not rule out CKD.

Nutritional Management

Nutritional management can be more challenging in senior pets (ie, those >7 years of age) because they often have several concurrent disorders; however, nutritional management should be considered for senior patients with CKD and weight loss and may be helpful in arthritis cases. Nutritional management for feline IRIS Stage 1 CKD is less clear-cut than for later stages, but there are some key guidelines (see *Feline IRIS Stage 1 CKD Guidelines*).¹

Recommendations vary regarding dietary phosphorus restriction in patients with early CKD; however, the diet should not be high in phosphorus. A nonacidifying, low-sodium diet with increased water-soluble vitamins is appropriate. Although low-sodium diets are not associated with hypertension in cats, high salt is associated with hypokalemia and possibly an increase in serum creatinine, blood urea nitrogen, and phosphorus. The amount of protein to provide at IRIS Stage 1 is controversial. This patient—like many older cats—has muscle loss, so restriction should initially not be excessive, and a high-quality protein (ie, with a high percentage of essential amino acids) should be fed.² Omega-3 fatty acids may help improve survival time in patients with CKD,³ improve arthritis signs,⁴ and improve cognition in older cats.5

Transitioning to a new diet should be done slowly, with both the old and new diets offered initially. For this patient, the diets were mixed; however, some clinicians may recommend offering each diet separately based on the proportions an individual cat will accept. In some cases, it may take weeks to transition a cat to a new diet.

Warming a canned diet to just below body temperature may be helpful. Maropitant can help with nausea and vomiting, and mirtazapine can help stimulate appetite.

For this patient, a commercial diet formulated for older cats is appropriate. A senior diet can be a good transition diet for cats with early stages of CKD. Many senior diets are lower in phosphorus and sodium and are less acidic than maintenance diets. Potassium content should be high, as there will be increased renal loss. Antioxidants are often added to help enhance immune and cognitive function and increase longevity. Oxidative damage may be present in renal disease, and antioxidants may have a beneficial effect on this stress.⁶

A diet with functional lipids (fish oil), antioxidants (vitamins C and E), L-carnitine, botanicals (vegetables), highly bioavailable protein, and amino acid supplements was shown to improve symmetrical dimethylarginine (SDMA) in older cats.⁷ A dose of EPA and DHA of 50-100 mg/kg has been suggested, as long as it does not affect diet palatability.⁷ Older cats should have an energy-dense diet (4-4.5 kcal/g dry matter). Caloric intake should only be restricted in obese cats.

FELINE IRIS STAGE 1 CKD GUIDELINES¹

- ▶ Adequate fluid intake can prevent dehydration. Feeding canned food and providing multiple accessible water sources may help with hydration. Water bowls should be easily accessible, especially for cats with arthritis, and should be separate from the food bowl and the litter box.
- ▶ A palatable diet can help prevent further weight loss.
- Phosphorus should be restricted to decrease renal secondary hyperparathyroidism.
- Excess sodium should be avoided.
- Acidifying diets should be avoided, as metabolic acidosis may be present.
- Water-soluble vitamin supplementation can replace vitamins lost in urine.
- ► High-quality protein (ie, proteins with a high percentage of amino acids), possibly in reduced amounts, can decrease azotemia.
 Continues ►

ASK YOURSELF...

QUESTION 1

What percentage of body weight has this patient lost in the last 18 months?

A. 1%

B.5%

C. 10%

D. 20%

MOST ACCURATE ANSWER: C

A 10% loss of body weight over a prolonged period is considered significant and likely indicates a problem. This should be addressed, especially in older cats, as it can be a poor prognosticator for survival time.

QUESTION 2

What test might be recommended to diagnose early renal disease in this cat?

A. Bile acid stimulation test

B. Inulin clearance test

C. SDMA

D. Water-deprivation test

MOST ACCURATE ANSWER: C

SDMA is a blood test that detects renal disease earlier than a serum creatinine test. Bile acids are not related to renal function. Inulin clearance tests are more difficult, and water-deprivation testing would be contraindicated.

QUESTION 3

This patient has lost weight but still has a BCS of 6/9. Should weight loss be advised?

- A. Yes, excess body weight may worsen his arthritis and increase his risk for diseases such as diabetes mellitus.
- B. No, intentional weight loss is not indicated in a cat with CKD, especially one that already has unintentional weight loss.

MOST ACCURATE ANSWER: B

This cat should not lose weight; maintaining or even gaining a bit of weight (especially as muscle mass) is consistent with longer survival times in cats with CKD.

QUESTION 4

In feline CKD, it is important to restrict dietary:

A. Carbohydrates

B. Fat

C. Phosphorus

D. Magnesium

MOST ACCURATE ANSWER: C

In CKD, phosphorus elimination via the kidneys is decreased, and parathyroid hormone will increase as the body attempts to increase its excretion. Increased parathyroid hormone functions as a uremic toxin, so dietary phosphorus restriction is recommended in most cases.

OUESTION 5

Senior diets for cats should have:

A. Decreased antioxidants

B. Increased caloric density

C. Increased phosphorus

D. Increased magnesium

MOST ACCURATE ANSWER: B

Older cats are often less able to use nutrients than are younger cats and do not absorb fats and protein as well. They are more likely to lose weight, so many senior diets have increased caloric density. These diets are often lower in phosphorus and contain more antioxidants as compared with adult maintenance diets.

See page 95 for references.

QUARTERLY UPDATE

SPRING 2018



LEADING THE FIGHT AGAINST HEARTWORM DISEASE

OVERCOMING THE OBSTACLES TO CARE



STEPHEN JONES, DVM IMMEDIATE PAST PRESIDENT, AMERICAN HEARTWORM SOCIETY LAKESIDE ANIMAL HOSPITAL MONCKS CORNER, SOUTH CAROLINA

Why Don't Clients Give Heartworm Preventives?

hile pet numbers in the U.S. are increasing, the number of annual heartworm preventive doses sold in the U.S. is declining. I believe this is a frightening trend, especially considering that the average number of heartworm cases per veterinary clinic rose by 21% between 2013 and 2016.¹

I recently researched medication adherence in human patients² in order to better understand why people don't take their own medications. In the process, I learned that the reasons my clients don't give pets heartworm preventives as directed are similar to the reasons they skip their own cholesterol, diabetes and blood pressure medications.



FORGETFULNESS. One in four patients says they miss taking medications because they forget, and I've found forgetfulness to be the most common reason my clients skip or miss doses of heartworm preventives, too. No matter how easy it may be to administer preventives, an action taken once a month or twice a year isn't necessarily frequent enough to become habitual. That's why

most owners need an external reminder, such as a text, email or calendar alert. If we want owners to give heartworm preventives on time, every time, we need to build a reminder into every prescription.



COST. Expense is a leading reason people don't fill their prescriptions or purchase refills, and it's a real concern for pet owners, too—especially if they live on fixed incomes or have multiple pets. I address cost in several ways:

(1) I inform owners when less-expensive options are available; (2) I give the owner the option to buy fewer doses of medication at a time; and (3) I explain

that failure to give heartworm preventives—or to give them year-round—can result in treatment that costs many times that of giving preventives.



FEAR. People worry about medication side effects. Their anxiety might not be based on experience; in fact, many concerns are based on stories people hear or read. When clients voice concerns like these, I remind them that today's preventive medications are extremely safe, and I reeducate them about how deadly heartworm infection can harm their pets.



MISUNDERSTANDING. Patients and owners who don't understand the reason for a medication are much less likely to take or give it as directed. With a disease like heartworm, which has subtle symptoms, it's especially important to educate owners about the disease, as well as how their preventive medication works.

Owners may have these and other reasons for poor adherence, but the answer is always the same. Take the time to educate your clients about every aspect of heartworm prevention—and repeat as needed.

For more information on this and other heartworm topics, visit heartwormsociety.org

¹2016 American Heartworm Society Incidence Survey

² Adherence and Health Care Costs, A Luga, MJ McGuire. Risk Manag Healthc Policy, 2014; 7: 35–44.

Osurnia[™]

(florfenicol • terbinafine • betamethasone acetate)

Otic gel

Antibacterial, antifungal, anti-inflammatory

For Otic Use in Dogs Only

Caution:

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

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

Indication:

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

Dosage and Administration:

OSURNIA should be administered in the clinic. Clean and dry the external ear canal before administering the initial dose of the product. Administer one dose (1 tube) per affected ear(s) and repeat administration in 7 days. Do not clean the ear canal for 45 days after the initial administration to allow contact of the gel with the ear canal. Cleaning the ear may affect product effectiveness (see **Effectiveness**). If alternative otic therapies are required it is recommended to clean the ear(s) before application. Open tube by twisting the soft tip. Insert the flexible tip into the affected external ear canal(s) and squeeze entire tube contents into the external ear canal(s). After application, gently massage the base of the ear to allow the gel to penetrate to the lower part of the ear canal.

See product insert for complete dosing and administration information

Contraindications:

Do not use in dogs with known tympanic perforation (see **Precautions**).

Do not use in dogs with a hypersensitivity to florfenicol, terbinafine or corticosteroids.

Warnings:

Not for use in humans. Keep this and all medications out of reach of children. Consult a physician in case of accidental ingestion by humans. In case of accidental skin contact, wash area thoroughly with water. Avoid contact to the eyes.

Precautions:

Do not administer orally.

The use of OSURNIA in dogs with perforated tympanic membranes has not been evaluated. The integrity of the tympanic membrane should be confirmed before administering this product. Reevaluate the dog if hearing loss or signs of vestibular dysfunction are observed during treatment.

Use of topical otic corticosteroids has been associated with adrenocortical suppression and iatrogenic hyperadrenocorticism in dogs (see **Animal Safety**).

Use with caution in dogs with impaired hepatic function (see **Animal Safety and Adverse Reactions**).

The safe use of OSURNIA in dogs used for breeding purposes, during pregnancy, or in lactating bitches, has not been evaluated.

Adverse Reactions:

The following adverse reactions were reported during the course of a US field study for treatment of otitis externa in dogs treated with OSURNIA with 1 tube per affected ear(s) and repeated after 7 days:

Frequency of Adverse Reaction by Treatment

Adverse Reaction		
	OSURNIA (n=190)	Placebo (n=94)
Elevated Alkaline Phosphatase	15 (7.9%)	3 (3.2%)
Vomiting	7 (3.7%)	1 (1.1%)
Elevated AST, ALT, ALP*	2 (1.1%)	0 (0.0%)
Weight loss (>10% body weight)	1 (0.53%)	0 (0.0%)
Hearing Decrease/Loss	1 (0.53%)	1 (1.1%)

*Aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP). Two dogs with pre-existing elevations in ALP were reported to have an increase in liver enzymes (ALP, ALT and/or AST) at study exit. Subsequent clinical chemistries returned to pre-treatment levels in one dog, while no follow up was performed for the second dog.

Effectiveness:

Effectiveness was evaluated in 235 dogs with otitis externa. The study was a double-masked field study with a placebo control (vehicle without the active ingredients). One hundred and fifty-nine dogs were treated with OSURNIA and seventy-six dogs were treated with the placebo control. All dogs were evaluated for safety. Treatment (1 mL) was administered to the affected ear(s) and repeated 7 days later. Prior to the first administration, the ear(s) were cleaned with saline but not prior to the Day 7 administration. Six clinical signs associated with otitis externa were evaluated: pain, erythema, exudate, swelling, odor and ulceration. Total clinical scores were assigned for a dog based on the severity of each clinical sign on Days 0, 7, 14, 30 and 45. Success was determined by clinical improvement at Day 45. The success rates of the two groups were significantly different (p=0.0094); 64.78% of dogs administered OSURNIA were successfully treated, compared to 43.42% of the dogs in the placebo control group.

Storage Conditions:

OSURNIA should be stored under refrigerated conditions between 36° - 46° F (2° - 8° C). To facilitate comfort during administration, OSURNIA may be brought to room temperature and stored for up to three months.

How Supplied:

OSURNIA is a gel in a single use tube with a flexible soft tip, supplied in cartons containing 2 or 20 tubes.

NADA # 141-437, Approved by FDA

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Elanco US Inc. Greenfield, IN 46140, USA

Product of Great Britain

10/16



PA100451AMX_BrS1 P1:





APPLIES LIKE A LIQUID STAYS LIKE A GEL

Choose the otitis externa solution that goes AND stays
where you need it for increased contact
time at the source of infection.

INDICATION

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

IMPORTANT SAFETY INFORMATION

OSURNIA® (florfenicol/terbinafine/betamethasone acetate) is for otic use only under veterinary supervision. Do not use in dogs with known tympanic perforation or a hypersensitivity to florfenicol, terbinafine or corticosteroids. Adverse reactions observed during clinical trials include vomiting, increased liver enzymes and transient loss of hearing. Please see Brief Summary of Full Prescribing Information on 68.



Blood Smear Platelet Evaluation & Interpretation

Lisa M. Pohlman, DVM, MS, DACVP Kansas State University

In most laboratories and veterinary practices, platelet concentration is determined via automated analysis. However, there are several variables that can affect accuracy of results, the most common of which, in the author's experience, is platelet clumping. Platelet clumps must be identified on a blood film to avoid potential misdiagnosis of thrombocytopenia.

Analyzers that use impedance methodology can also produce erroneous results when platelet size overlaps with RBC size, causing large platelets to be counted as RBCs; this can result in a falsely decreased platelet concentration and misdiagnosis. This can occur in any animal that produces large platelets but is particularly common in cats, as their platelet size is similar to their RBC size.^{1,2}

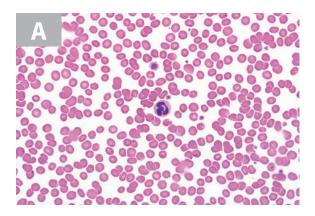
Estimation of the platelet concentration from a blood film should be performed in the monolayer using

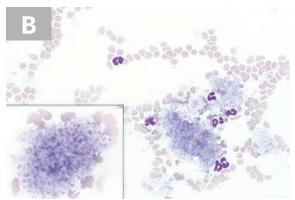
100× objective (ie, 1000× magnification). A well made blood film with even distribution of platelets throughout the monolayer is essential. If platelet clumps are present, the platelet estimation will be falsely decreased to an unknown degree, depending on the amount of clumping. However, estimation using the method provided should help to provide the minimum concentration of platelets present.

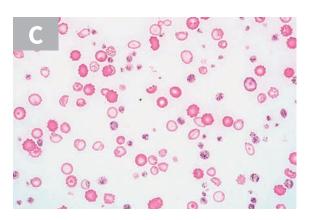
First, the entire film should be examined for clumps. Then, at least 10 fields within the monolayer should be reviewed to determine the average number of platelets per 1000× magnification field. The number observed should be multiplied by 15 000 to get the lower end of the reference interval and then by 20 000 to determine the upper end of the reference interval.²

Average number of platelets per 1000× field × 15 000 = lower end of reference interval Average number of platelets per 1000× field × 20 000 = upper end of reference interval

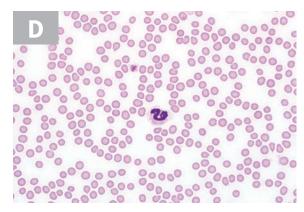
> $10 \times 15\ 000 = 150\ 000/\mu L$ $10 \times 20\ 000 = 200\ 000/\mu L$

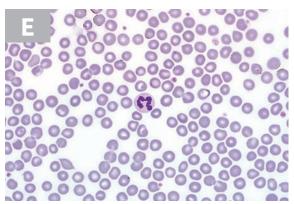






Although individual laboratory reference values vary, healthy dogs and cats typically have 150 000 to 500 000 platelets/µL.





MATCH THE IMAGES

Match the images with the correct interpretation.

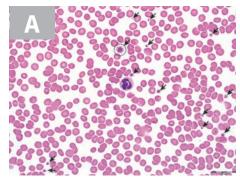
Although individual laboratory reference values vary, healthy dogs and cats typically have 150 000 to 500 000 platelets/ μL . For the purposes of this article, less than 150 000/ μL is indicative of thrombocytopenia and greater than 500 000/ μL is indicative of thrombocytosis. Of note, the purpose of this exercise is to demonstrate the method of platelet estimation; because the images in this exercise are square, they may not be representative of the number of platelets seen in an entire 1000× magnification field. All films are stained with modified Wright's Stain.

- ___ Platelet clumps
- ___ Thrombocytosis
- ___ Thrombocytopenia in a cat
- ___ Platelet concentration within reference limits (dog)
- ___ Platelet concentration within reference limits (cat)

ANSWER KEY

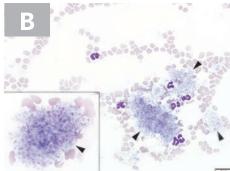
Platelet concentration within reference limits (cat)

This blood film (1000× magnification) from a cat shows 13 platelets (arrows). No platelet clumps are evident on the smear. A large platelet (circle), which is typical of cat blood, can be observed. With the assumption that this field is representative of other 1000× fields within the monolayer, the estimated platelet concentration would be 195 000/ μ L to 260 000/ μ L.



Platelet clumps

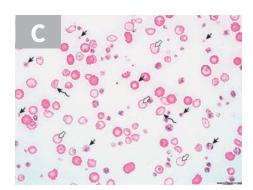
Platelet clumps (*arrowheads*) at the feathered edge of the blood film (600×) can be observed in this blood film from a cat. The inset image shows another platelet clump at high power (1000× oil).





Thrombocytosis

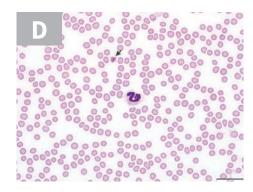
There are 71 platelets in this field (some indicated by black arrows) from a blood film (1000×) from a dog. Using the formula provided and assuming that there are no platelet clumps and that this field of view is representative of other fields, the estimated platelet concentration is $1065000/\mu$ L to $1420000/\mu$ L. This dog had a severe iron deficiency; marked hypochromasia (ie, increased central pallor; white arrows) and thin RBCs (ie, leptocytes; curved arrows) can be seen; RBCs are often folded due to a lack of internal contents. Reactive thrombocytosis is a common CBC finding in patients with iron deficiency.^{2,3}



<u>D</u>

Thrombocytopenia

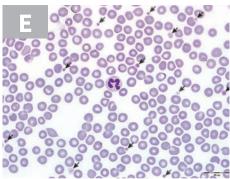
This field from a blood film (1000×) from a cat shows a large platelet (*arrow*). Assuming that there are no platelet clumps and that this field of view is representative of other fields, the estimated platelet concentration is low at 15 000/ μ L to 20 000/ μ L.



Ε

Platelet concentration within reference limits (dog)

Blood film from a dog ($1000 \times$ magnification). Twelve platelets (*arrows*) can be observed. Note the central pallor in the majority of the RBCs, which is a normal finding in dogs.⁴ Assuming that there are no platelet clumps in the sample and that this field of view is representative of other fields in the monolayer, the estimated platelet concentration would be $180\ 000/\mu$ L to $240\ 000/\mu$ L.



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LOOK FOR THESE RELATED ARTICLES IN FUTURE ISSUES

- Image Gallery: Blood Smear Evaluation of White Blood Cells
- Image Gallery: Blood Smear Evaluation of Red Blood Cells



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Top 5 Gastrointestinal & Hepatobiliary **Antibiotics**

Craig B. Webb, PhD, DVM, DACVIM Colorado State University



Antibiotic use in GI and hepatobiliary disease should be judicious, purposeful, and, ideally, directed by culture and susceptibility results when appropriate. These conditions are often chronic or recurring, and repeated courses of ineffective or unnecessary antibiotic "trials" could result in the emergence of antibioticresistant organisms. Injudicious use of common antibiotics can also be associated with significant alterations in the microbiota, risking both immediate and far-reaching deleterious consequences.1

The author considers enrofloxacin, metronidazole, and tylosin to be the antibiotics most deserving of thoughtful consideration in the treatment of GI conditions in dogs and cats. Metronidazole and enrofloxacin are also frequently used in the treatment of hepatic disease. Amoxicillin-clavulanic acid and neomycin are additional important antibiotics for pharmacotherapy of hepatobiliary conditions.

Enrofloxacin Enrofloxacin is a fluoroquinolone with broad-spectrum bactericidal activity against aerobic bacteria. Its mechanism of action is believed to be inhibition of bacterial DNA-gyrase, which then prevents DNA supercoiling and synthesis.2 Enrofloxacin also has efficacy against Escherichia coli.

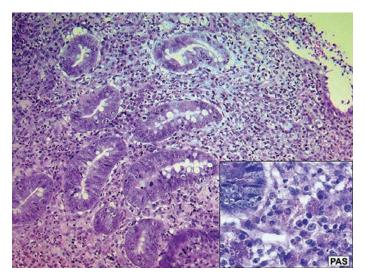
Enrofloxacin represents a unique collective effort of the veterinary profession to successfully identify a specific therapy targeting a defined condition (ie, histiocytic

TOP 5 **GASTROINTESTINAL** & HEPATOBILIARY **ANTIBIOTICS**

- 1. Enrofloxacin
- 2. Metronidazole
- 3. Tylosin
- 4. Amoxicillin-Clavulanic Acid
- 5. Neomycin

March 2018

ulcerative colitis [HUC; Figure 1] in boxers) that previously had been almost always terminal. This accomplishment serves as an example of the effort that should inform all areas of antibiotic use in small animal medicine, 3-6 particularly because of the therapeutic difficulties now presented by antibiotic resistance. Before enrofloxacin was identified as an effective treatment for HUC, most boxers with this disease were euthanized because immunosuppressive therapy was unable to slow the rapid progression of the condition. Invasive *E coli* was identified as the causal agent, and remission was correlated with eradication of intramucosal E coli organisms following treatment with enrofloxacin (5-10 mg/kg PO q24h for 6-8 weeks).⁷⁻⁹ Cases of HUC in which enrofloxacin was a critical component of successful therapy have also been reported in French bulldogs, an English bulldog, and several other nonboxer breeds. $^{10-12}$ It is crucial to note that treating dogs with enrofloxacin before obtaining a definitive diagnosis of HUC has been associated with antimicrobial resistance and a poor clinical outcome.¹³



▲ FIGURE 1 Histopathology and Periodic Acid-Schiff (PAS) stain of a sample obtained from a dog with histiocytic ulcerative colitis

E coli is one of many potential enteropathogenic bacteria associated with GI disease in dogs and cats; however, according to the ACVIM Consensus Statement on enteropathogenic bacteria, the disease is uncomplicated and self-limiting in most cases, molecular identification is sophisticated but causality is extremely elusive, and the injudicious use of antibiotics in GI disease may cause more harm than benefit.14

The most common adverse effects of enrofloxacin are GI in nature, including vomiting, diarrhea, and loss of appetite. Enrofloxacin should not be used in young, growing dogs because of the risk for cartilage damage. Enrofloxacin should be avoided in patients with seizure disorders and used at a reduced dose in patients with a significant loss of renal or hepatic function. Enrofloxacin should not be used at dosages greater than 5 mg/kg/day in cats because of the retinotoxicity reported in this species.²

Metronidazole Metronidazole is a bactericidal antibiotic that targets anaerobes; it is also an antiprotozoal agent used frequently to treat *Giardia* spp infection. It is one of the most common nonspecific antidiarrheal drugs prescribed in veterinary medicine. 15,16 Metronidazole has been shown to have immunomodulatory effects in mice (in vitro) and in humans, and these properties often are cited as justification for its use as a nonspecific GI immunosuppressive agent.¹⁷⁻¹⁹ However, recent work in a model of sepsis failed to identify any impact of metronidazole on systemic innate immune responses in humans.²⁰

The veterinary profession's understanding and appreciation for the importance of the microbiota for GI health and immune function is increasing, along with concern over the untargeted use of antibiotics and their potential for contributing to dysbiosis, and metronidazole is a key component of this discussion. Metronidazole (12.5 mg/kg PO q12h for 14 days) has been shown to reduce some pathogenic bacteria (eg, fusobacteria) and increase some beneficial bacteria (eg, bifidobacteria) but also significantly decrease the bacterial composition and diversity of the microbiota of healthy dogs. ²¹ Composition and diversity are thought to be central components of a healthy microbiome. Recent studies have demonstrated significant dysbiosis and decreased microbiota diversity in dogs with both acute diarrhea and inflammatory bowel disease. ^{22,23}

Metronidazole has been used in the treatment of a number of veterinary diseases but most often in combination with other therapeutic agents, making it difficult to assess the efficacy of the antibiotic alone. Metronidazole (15-20 mg/kg PO q12h for 7-17 days) was found to effectively resolve diarrhea in an outbreak of Clostridium difficile-toxinpositive dogs at a small animal teaching hospital.²⁴ In a recent report, metronidazole (10 mg/kg PO q12h for 5 days) was used in combination with trimethoprim-sulfamethoxazole in Labrador retriever puppies presented for anorexia, hematemesis, and hematochezia and diagnosed with Isospora spp infection. All puppies recovered completely.²⁵ In another report, metronidazole (10-15 mg/kg PO q12h for 6 weeks) was used in combination with prednisolone in a group of dogs presented for diarrhea and vomiting with hypoalbuminemia and hypocobalaminemia. Colonoscopy and histopathology showed lipogranulomatous lymphangitis, and fluorescent in situ hybridization (FISH) analysis disclosed invasive bacteria in 20% of the cases. Remission was achieved in 8 of the 10 dogs.²⁶ Another paper, however, reported that combining metronidazole (10 mg/kg PO) with prednisone was no more effective as induction therapy for dogs with inflammatory bowel disease than using prednisone alone.27 A 2007 paper described the use of metronidazole (10 mg/kg PO q12h for 2 weeks) as part of a triple antimicrobial therapy in dogs with chronic vomiting and gastric Helicobacter spp infection. Vomiting frequency was reduced by 86%.28

Exposure to antibiotics, including metronidazole or fluoroquinolones, markedly increases the risk for new-onset irritable bowel disease, specifically

Crohn's disease, especially in children.²⁹ Of increasing concern is the emergence of metronidazole-resistant organisms,³⁰ as was demonstrated in one study that found metronidazole-resistant *C difficile* isolates in dogs with GI disorders.³¹ Metronidazole is frequently prescribed for treatment of hepatic encephalopathy in dogs and cats, but controlled clinical trials evaluating the effectiveness of this therapy in veterinary patients have not been conducted.³²

Tylosin

Tylosin is a macrolide antibiotic thought to bind 50S ribosomes and inhibit protein synthesis. It is frequently used as adjunct treatment for diarrhea in veterinary patients with a variety of diseases. A specific GI condition in dogs termed tylosin-responsive diarrhea has been identified in middle-aged, large-breed dogs with chronic diarrhea that resolves rapidly following tylosin treatment but returns just as quickly with the cessation of tylosin treatment.³³ A subsequent study found that the combination of tylosin (20 mg/kg PO q24h for 10 days) and a highly digestible canned food diet effectively controlled chronic diarrhea for at least 3 months in a group of beagles.³⁴ In a randomized placebo-controlled clinical trial in dogs, recurrent diarrhea that had previously resolved with tylosin treatment responded to tylosin again in 85% of cases (25 mg/kg PO q24h for 7 days).35

Metronidazole has been used in the treatment of a number of veterinary diseases but most often in combination with other therapeutic agents, making it difficult to assess the efficacy of the antibiotic alone.

HUC = histiocytic ulcerative colitis

Later work suggested that a dose as low as 5 mg/kg PO q24h for 7 days may be just as effective in cases of relapsing diarrhea.³⁶ In a translational study, a 10-day course of tylosin significantly improved diarrhea, decreased colonic inflammation, and decreased serum C-reactive protein levels in rhesus macaques with chronic diarrhea.³⁷

Tylosin (20-22 mg/kg PO q24h for 14 days) may resolve diarrhea because it increases concentrations of *Enterococcus* spp- and *E coli*-like organisms while decreasing fusobacteria and Bacteroidales in the jejunum of healthy dogs. 38 A study of dogs with recurrent tylosin-responsive diarrhea found that tylosin administration significantly increased Enterococcus spp in those dogs with diarrhea that resolved following administration of tylosin (25 mg/kg PO q24h for 7 days).39

Like metronidazole, tylosin is often used for properties believed to be immunomodulatory.

TABLE

COMMON BACTERIA CAUSING BACTERIAL CHOLANGITIS IN DOGS & CATS

Bacterium	Class	
Common		
Escherichia coli	Gram-negative aerobic	
Enterococcus spp	Gram-positive aerobic	
Clostridium spp	Anaerobic	
Streptococcus spp	Gram-positive aerobic	
Rare		
Enterobacter spp	Gram-negative aerobic	
Klebsiella spp	Gram-negative aerobic	
Proteus spp	Gram-negative aerobic	
Bacteroides spp	Anaerobic	

Although tylosin has not been shown to demonstrate such properties, studies of the macrolide antibiotic tilmicosin in large animals suggest that it has immunomodulatory and anti-inflammatory properties. 40 Tylosin is one of the most frequently prescribed medications for dogs with irritable bowel disease.41

Amoxicillin-Clavulanic Acid Amoxicillin-clavulanic acid is a bactericidal aminopenicillin with a β -lactamase inhibitor. Penicillins act by inhibiting cell wall synthesis. Adverse effects are rarely serious, although GI signs (eg, anorexia, vomiting, diarrhea) are relatively common.

Studies published in 2007 and 2016 demonstrated that bacterial cholangitis and cholecystitis (*Table*), although rarely reported in the literature, should be considered in dogs and cats presented for vomiting, jaundice, and abdominal pain and/or fever. 42,43 These patients commonly have an increase in liver enzyme activity, hyperbilirubinemia, an inflammatory leukogram, and ultrasonographic evidence of gallbladder abnormalities. Because antimicrobial resistance has become common with aerobic isolates, antibiotic choice should be based on culture and susceptibility testing. Sampling the bile or gallbladder wall—not the liver—results in the greatest yield for a positive culture. In these studies, metronidazole was used to treat most anaerobic infections, whereas a fluoroquinolone (eg, enrofloxacin, ciprofloxacin) or amoxicillin-clavulanic acid was used to treat most patients with aerobic infection. In the absence of antimicrobial susceptibility testing, treatment with a broad-spectrum antibiotic is indicated and may require combination of a fluoroquinolone, penicillin, and metronidazole or a fluoroquinolone and amoxicillin-clavulanic acid. Use of empiric therapy may fail because of the prevalence of antimicrobial resistance in the common isolates.42,43

According to the WSAVA International Liver Standardization Group, feline cholangitis is the predominant liver disease in cats after hepatic

lipidosis.44 In cases of acute neutrophilic cholangitis, a bacterial infection is likely the inciting cause, and many of these cats are presented with significant clinical morbidity.⁴⁵ Clinical signs include acute onset of vomiting, diarrhea, anorexia, and lethargy, and patients may be febrile and icteric (*Figure 2*). These cats may have pancreatitis and gastroenteritis as concurrent conditions (feline triaditis), and aggressive supportive care along with directed antibiotic therapy may be critical to a successful outcome. Gallbladder aspiration for cytology (Figure 3) and culture has become the diagnostic test of choice in these cases, and culture and susceptibility results should dictate the choice of antibiotic. 46,47 The bacteria most frequently identified in feline neutrophilic cholangitis are enteric organisms (Figure 4), including E coli, Enterococcus spp, Bacteroides spp, Clostridium spp, and Streptococcus spp. 48 In lieu of culture and susceptibility results, empiric therapy with amoxicillinclavulanic acid for 8 weeks is recommended.⁴⁹

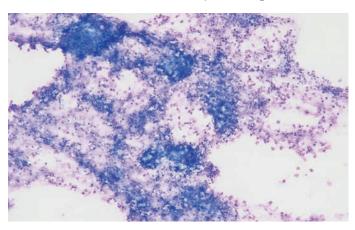
Neomycin

An important potential clinical consequence of decreased liver function is hepatic encephalopathy. In dogs and cats, hepatic encephalopathy is most commonly associated with portosystemic shunts (congenital or acquired), portal hypertension or liver cirrhosis (eg, from chronic copper hepatopathy), and, more rarely, acute hepatic failure (eg, from drugs and toxins). Although the pathogenesis is not completely understood, intestinal bacteria are thought to represent an important source of ammonia production, and increased systemic ammonia concentrations play a central role in this condition. 50

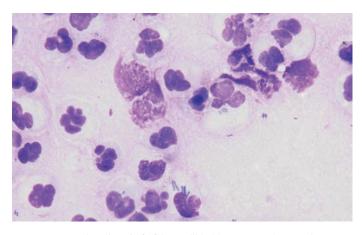
Urease-producing bacteria in the GI tract convert urea to ammonia. One treatment strategy uses antibiotics to change the GI microbiota in a way that decreases bacterial production of ammonia. The importance of the microbiota to ammonia production was highlighted by a study showing that probiotic therapy resulted in a significant reduction in overt encephalopathy in humans with liver cirrhosis.⁵¹



▲ FIGURE 2 Icterus in a cat with acute neutrophilic cholangitis



▲ FIGURE 3 Cytology (10×) of a gallbladder aspirate showing inflammation in a cat with acute neutrophilic cholangitis. Image courtesy of Laureen Peters, Dr. med. vet, MVetMed, MRCVS, DACVP, Royal Veterinary College



▲ FIGURE 4 Cytology (100×) of a feline gallbladder aspirate showing the bacterial etiology (enteric organisms, rods) of acute neutrophilic cholangitis. Image courtesy of Laureen Peters, Dr. med. vet, MVetMed, MRCVS, DACVP, Royal Veterinary College

Neomycin is a bactericidal aminoglycoside that binds to the 70S ribosomal subunit. In dogs and cats, oral neomycin (20 mg/kg PO q8-12h) is still used in conjunction with lactulose for treating hepatic encephalopathy, although, as in humans, both nephrotoxicity and ototoxicity are serious concerns. Metronidazole (7.5 mg/kg PO q8h or q12h) has been used as an alternative antibiotic in veterinary patients.²

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Continues on page 93



Flavored chews for dogs

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

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

Indications:

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

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

Contraindications:

There are no known contraindications for the use of the product.

Warnings:

Not for human use. Keep this and all drugs out of the reach of children. Keep the product in the original packaging until use, in order to prevent children from getting direct access to the product. Do not eat, drink or smoke while handling the product. Wash hands thoroughly with soap and water immediately after use of the product.

Precautions

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

Adverse Reactions:

In a well-controlled U.S. field study, which included 294 dogs (224 dogs were administered Bravecto every 12 weeks and 70 dogs were administered an oral active control every 4 weeks and were provided with a tick collar); there were no serious adverse reactions. All potential adverse reactions were recorded in dogs treated with Bravecto over a 182-day period and in dogs treated with the active control over an 48-day period. The most frequently reported adverse reaction in dogs in the Bravecto and active control groups was vomiting.

Percentage of Dogs with Adverse Reactions in the Field Study

Adverse Reaction (AR)	Bravecto Group: Percentage of Dogs with the AR During the 182-Day Study (n=224 dogs)	Active Control Group: Percentage of Dogs with the AR During the 84-Day Study (n=70 dogs)
Vomiting	7.1	14.3
Decreased Appetite	6.7	0.0
Diarrhea	4.9	2.9
Lethargy	5.4	7.1
Polydipsia	1.8	4.3
Flatulence	1.3	0.0

In a well-controlled laboratory dose confirmation study, one dog developed edema and hyperemia of the upper lips within one hour of receiving Bravecto. The edema improved progressively through the day and had resolved without medical intervention by the next morning.

For technical assistance or to report a suspected adverse drug reaction, contact Merck Animal Health at 1-800-224-5318. Additional information can be found at www. bravecto.com. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at http://www.fda.gov/AnimalVeterinary/SafeyHealth.

How Supplied:

Bravecto is available in five strengths (112.5, 250, 500, 1000, and 1400 mg fluralaner per chew). Each chew is packaged individually into aluminum foil blister packs sealed with a peelable paper backed foil lid stock. Product may be packaged in 1, 2, or 4 chews per package.

Distributed by:

Intervet Inc (d/b/a Merck Animal Health)

Madison, NJ 07940

Made in Austr

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NADA 141-459, Approved by FDA



(fluralaner topical solution) for Dogs

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

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

Indications:

Bravecto kills adult fleas and is indicated for the treatment and prevention of flea infestations (*Cenocephalides felis*) and the treatment and control of tick infestations [*brodes scopularis* (black-legged tick), *Dermocentor variabilis* (American dog tick), and *Rhipicephalus songuineus* (brown dog tick)] for 12 weeks in dogs and puppies 6 months of age and older, and weighing 4.4 pounds or greater.

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

Contraindications:

There are no known contraindications for the use of the product.

WARNINGS

Human Warnings:

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

The product is highly flammable. Keep away from heat, sparks, open flame or other sources of ignition.

Precautions:

For topical use only. Avoid oral ingestion. Use with caution in dogs with a history of seizures. Seizures have been reported in dogs receiving fluralaner, even in dogs without a history of seizures. Bravecto has not been shown to be effective for 12-weeks duration in puppies less than 6 months of age. Bravecto is not effective against Amblyomma omericanum ticks beyond 8 weeks after dosing.

Adverse Reactions:

In a well-controlled U.S. field study, which included a total of 165 households and 321 treated dogs (221 with fluralaner and 100 with a topical active control), there were no serious adverse reactions.

Percentage of Dogs with Adverse Reactions in the Field Study

Adverse Reaction (AR)	Bravecto Group: Percent of Dogs with the AR During the 105-Day Study (n=221 dogs)	Control Group: Percent of Dogs with the AR During the 84-Day Study (n=100 dogs)
Vomiting	6.3%	6.0%
Alopecia	4.1%	2.0%
Diarrhea	2.7%	11.0%
Lethargy	2.7%	2.0%
Decreased Appetite	1.4%	0.0%
Moist Dermatitis/Rash	0.9%	0.0%

In the field study, two dogs treated with Bravecto with no prior history of seizures each experienced a seizure. One dog had two seizures a day apart about 18 days after its first dose. The dog was started on antiepileptic medication and had no additional seizures during the study. A second dog had a seizure 76 days after its first dose and 3 days after starting fluoxetine for separation anxiety. The fluoxetine was discontinued and the dog experienced no additional seizures during the study. One dog treated with Bravecto was observed by the owner to be off balance for about 30 minutes five days after its first dose and had no similar observations after the second dose. One dog with a history of seizures had a seizure the day after the second dose of the active control.

In two well-controlled laboratory dose confirmation studies, one dog developed mild to moderate redness, flaking, crusts/scabs and alopecia at the treatment site from Day 1 through 14 after application of Bravecto on Day 0, and one dog developed self-limiting generalized erythema (possible allergic reaction) one day after treatment with Braverto.

In a European field study in cats, there were three reports of facial dermatitis in humans after close contact with the application site which occurred within 4 days of application.

For technical assistance or to report a suspected adverse drug reaction, or to obtain a copy of the Safety Data Sheet (SDS), contact Merck Animal Health at 1-800-224-5318. Additional information can be found at www.bravecto.com. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at http://www.fda.gov/AnimalVeterinary/SafetyHealth.

How Supplied:

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

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155586 R4

NADA 141-459, Approved by FDA



(fluralaner topical solution) for Cats

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

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

Indications:

Bravecto kills adult fleas and is indicated for the treatment and prevention of flea infestations (*Clenocepholides felis*) and the treatment and control of *knodes scapularis* (black-legged tick) infestations for 12 weeks in cats and kittens 6 months of age and older, and weighing 2.6 pounds or greater.

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

Contraindications:

There are no known contraindications for the use of the product.

WARNINGS

Human Warnings:

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

with soap and water immediately after use of the product.

The product is highly flammable. Keep away from heat, sparks, open flame or other sources of ignition.

Precautions:

For topical use only. Avoid oral ingestion. Use with caution in cats with a history of neurologic ahonomalities. Neurologic abnormalities have been reported in cats receiving Bravecto, even in cats without a history of neurologic abnormalities. Bravecto has not been shown to be effective for 12-weeks duration in kittens less than 6 months of age. Bravecto is not effective against Dermacentor variabilist ticks beyond 8 weeks after dosing. The safety of Bravecto has not been established in breeding, pregnant and lactating cats.

Adverse Reactions:

In a well-controlled U.S. field study, which included a total of 161 households and 311 treated cats (224 with fluralaner and 87 with a topical active control), there were no serious adverse reactions.

Percentage of Cats with Adverse Reactions (AR) in the Field Study

Adverse Reaction (AR)	Bravecto Group: Percent of Cats with the AR During the 105- Day Study (n=224 cats)	Control Group: Percent of Cats with the AR During the 84-Day Study (n=87 cats)
Vomiting	7.6%	6.9%
Pruritus	5.4%	11.5%
Diarrhea	4.9%	1.1%
Alopecia	4.9%	4.6%
Decreased Appetite	3.6%	0.0%
Lethargy	3.1%	2.3%
Scabs/Ulcerated Lesions	2.2%	3.4%

In the field study, two cats treated with fluralaner topical solution experienced ataxia. One cat became ataxic with a right head tilt 34 days after the first dose. The cat improved within one week of starting antibiotics. The ataxia and right head tilt, along with lateral recumbency, reoccurred 82 days after administration of the first dose. The cat recovered with antibiotics and was redosed with fluralaner topical solution 92 days after administration of the first dose, with no further abnormalities during the study. A second cat became ataxic 15 days after receiving its first dose and recovered the next day. The cat was redosed with fluralaner topical solution 82 days after administration of the first dose, with no further abnormalities during the study.

In a European field study, two cats from the same household experienced tremors, lethargy, and anorexia within one day of administration. The signs resolved in both cats within 48-72 hours.

In a European field study, there were three reports of facial dermatitis in humans after close contact with the application site which occurred within 4 days of application.

For technical assistance or to report a suspected adverse drug reaction, or to obtain a copy of the Safety Data Sheet (SDS), contact Merck Animal Health at 1-800-224-5318. Additional information can be found at www.bravecto.com. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at http://www.fda.gov/AnimalVeterinary/SafetyHealth.

How Supplied:

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

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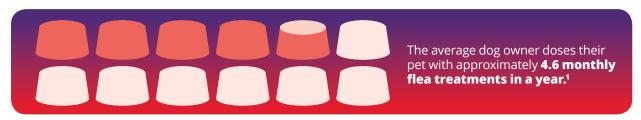




The challenge

Veterinarians recommend year-round flea and tick protection but...

Is everyone following the 12-month recommendation? No.



What do dog owners think? While...



of dog owners **agree** that their pets should have **12 months of flea and tick protection**²



of dog owners remembered their veterinarian's exact recommendation²

Brakke Consulting US Flea Control & Heartworm Markets report; 2015. ²Lavan et al. *Parasites & Vectors*. 2017; 10:284. ³Lavan et al. *J Vet Sci Technol*. 2017; 8:439.

*BRAVECTO Chew for Dogs [prescribing information]. Madison, NJ: Merck Animal Health; 2014.
*BRAVECTO Topical Solution for Dogs [prescribing information]. Madison, NJ: Merck Animal Health; 2016.

⁶BRAVECTO Topical Solution for Cats [prescribing information]. Madison, NJ: Merck Animal Health; 2016. ⁷Rohdich N, et al. *Parasites & Vectors*. 2014;7:83.

⁸Freedom of Information Summary, NADA 141-426. Approved May 15, 2014.

*BRAVECTO kills fleas and prevents flea infestations for 12 weeks. BRAVECTO Chew and BRAVECTO Topical Solution for Dogs kill ticks (black-legged tick, American dog tick, and brown dog tick) for 12 weeks and also kill lone star ticks for 8 weeks. BRAVECTO Topical Solution for Cats kills ticks (black-legged tick) for 12 weeks and American dog ticks for 8 weeks.

IMPORTANT SAFETY INFORMATION: BRAVECTO has not been shown to be effective for 12-weeks' duration in puppies or kittens less than 6 months of age. BRAVECTO Chew: The most common adverse reactions recorded in dinical trials were vomiting, decreased appetite, diarrhea, lethargy, polydipsia, and flatulence. BRAVECTO is not effective against lone star ticks beyond 8 weeks of dosing. BRAVECTO To pical Solution for Dogs: The most common adverse reactions recorded in clinical trials were vomiting, hair loss, diarrhea, lethargy, decreased appetite, and moist dermatitis/rash. BRAVECTO is not effective against lone star ticks beyond 8 weeks of dosing. For topical use only. Avoid oral ingestion. Use caution in dogs with a history of seizures. Seizures have been reported in dogs receiving fluralaner, even in dogs without a history of seizures. BRAVECTO To the process of dosing. For topical use only. Avoid oral ingestion. Use a caution in dogs with a history of seizures. BRAVECTO is not effective against American dog ticks beyond 8 weeks of dosing, For topical use only. Avoid oral ingestion. The safety of BRAVECTO has not been established in breeding, pregnant and lactating cals. Use with caution in cats with a history of neurologic abnormalities. Neurologic abnormalities have been reported in cats receiving BRAVECTO, even in cats without a history of neurologic abnormalities.

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Only **BRAVECTO** delivers up to **12 Weeks*** of flea and tick protection to dogs and cats with one convenient chew or topical dose.

Pet owners **prefer BRAVECTO** 9 to 1 over monthly treatments³



Fewer doses help improve adherence.



More convenient for pet owners



Fewer potential gaps in protection⁴⁻⁷



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93.2% of dogs ate BRAVECTO Chew voluntarily^{4,8}

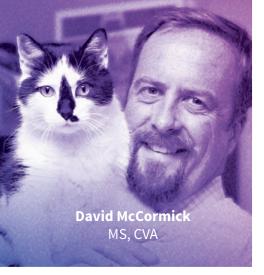
Available in topical applications for dogs and cats

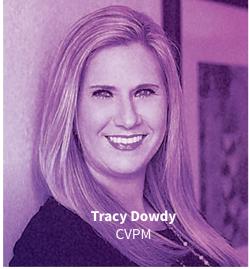
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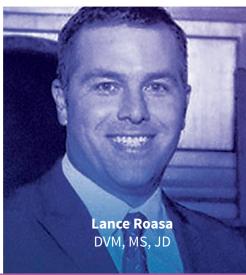




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Top 5 Corticosteroids for Use in **Emergency Settings**

Kiko E. Bracker, DVM, DACVECC Angell Animal Medical Center Boston, Massachussetts



Corticosteroids are a diverse group of medications used to treat a wide array of illnesses. At lower dose ranges, they provide antiinflammatory effects, whereas higher doses are immunosuppressive. These properties make them valuable tools in the emergency and critical care setting. Clinicians must be familiar with the appropriate indications for each drug, along with their relative potencies and adverse effects. Following are the author's top 5 corticosteroids used in emergency settings.

Prednisone/Prednisolone Prednisone is used for both anti-inflammatory and immunosuppressive purposes because of its effectiveness, low cost, small tablet size, innocuous taste, and variable dose sizes.

When used for anti-inflammatory effects, prednisone is administered at 0.5-1.0 mg/kg/day, often for only a few days to limit local or systemic inflammation.1-3 Inflammatory or traumatic disorders of emergency patients (eg, oropharyngeal trauma, oropharyngeal biopsy, decompensation secondary to laryngeal collapse or tracheal collapse) are often short in duration, and treatment with steroids for 2 to 3 days allows

TOP 5 **CORTICOSTEROIDS FOR USE IN EMERGENCY SETTINGS**

- 1. Prednisone/Prednisolone
- 2. Dexamethasone Sodium **Phosphate**
- 3. Hydrocortisone
- 4. Methylprednisolone Sodium Succinate
- 5. Fluticasone

the initial insult or exacerbation to subside. In patients with transient inflammatory disorders, the common side effects of steroids (see Glucocorticoid Adverse Effects) are mild because of the relatively low dose and short duration of treatment.³

Immunosuppressive doses of prednisone range from 1-2 mg/kg q12h.^{1,4} Some overlap of the dosing ranges for anti-inflammatory and immunosuppressive effects may be noted, most likely because those effects are not entirely distinct.

Steroids, particularly prednisone, are used to treat many autoimmune disorders, including immunemediated hemolytic anemia, immune-mediated thrombocytopenia, and immune-mediated polyarthropathy. Because these diseases often require long-term treatment with high doses of steroids, adverse effects are more common. A second or third immunosuppressive agent is often used with prednisone to maintain immunosuppression and allow rapid reduction of prednisone doses to maintenance levels.

Because cats and animals with severe hepatic disease have difficulty converting prednisone into the active

GLUCOCORTICOID ADVERSE EFFECTS

- ► Polyuria/polydipsia
- ► GI ulceration
- ► Increased liver enzyme activity
- ► Muscle atrophy
- ▶ Weakness
- Insulin resistance and hyperglycemia
- ► Symmetric hair loss
- ► Panting
- ► Polyphagia
- ► Impaired wound healing
- ► Hypercoagulability/thromboembolism

metabolite prednisolone, some sources suggest that prednisolone may be a better choice in these patients.^{5,6}

Dexamethasone Sodium Phosphate Dexamethasone is often used as the firstline steroid for urgent conditions because it has a rapid onset of action and can be administered parenterally.^{1,2} Most patients that require continued steroid therapy are switched to oral prednisone. Dexamethasone is approximately 7 times more potent than prednisone, so the prednisone dose should be approximately 7 times greater than an equivalent dexamethasone dose.^{1,2} For example, a patient receiving 5 mg dexamethasone would be switched to 30-35 mg prednisone.

When using different steroids, clinicians must be careful to recognize the relative glucocorticoid potency of each drug.^{1,2} Dexamethasone has a longer duration of action than other steroids. 1 When switching from injectable dexamethasone to an oral steroid, the oral steroid is usually started 24 hours after dexamethasone has been discontinued. Dexamethasone does not affect cortisol assays, so it can be administered to patients with suspected hypoadrenocorticism before an ACTH stimulation test or before blood is obtained for cortisol testing. However, continued use of dexamethasone (or any other steroid) will suppress the hypothalamic-pituitary-adrenal axis, which in turn will suppress endogenous cortisol concentrations.1

Hydrocortisone Many topical medications contain hydrocortisone as an anti-inflammatory agent. Even with topical application, some systemic absorption of hydrocortisone can occur.⁷ Hydrocortisone is used in shampoos and in various topical, ocular, and otic preparations to manage superficial irritation.

Hydrocortisone is also an appropriate treatment choice for critical illness-related corticosteroid insufficiency (CIRCI; formerly relative adrenal

insufficiency). CIRCI affects patients with severe sepsis that are hypotensive despite fluid therapy and vasopressor support. In some CIRCI patients, low doses of IV corticosteroids can improve blood pressure. Because there is no consensus on how best to diagnose this syndrome, an appropriate response to therapy is used as a surrogate for an objective diagnosis. The best treatment of CIRCI is not established, but hydrocortisone has been used at 0.5-1.0 mg/kg IV q6h or as a CRI at 2.5-3.0 mg/kg/day. If blood pressure improves within 24 hours of starting hydrocortisone, steroid supplementation should be continued at a tapering dose for approximately 1 week. 9,10

Methylprednisolone Sodium Succinate

IV methylprednisolone sodium succinate (MPSS) is often administered to dogs and cats with acute spinal cord injury before and after a decompressive spinal surgery. Strong opinions for and against the use of MPSS (and other steroids) exist within the veterinary community, despite the lack of evidence to support its benefits. 11,12 The human literature also shows little consensus regarding the use of MPSS for acute spinal cord injury.² The potential benefits of MPSS are likely associated with the limitation of ischemic and oxidative damage in the area of the damaged spine.² Side effects of aggressive MPSS therapy include diarrhea, vomiting, melena, hematemesis, and anorexia.¹³ MPSS should be considered only when it can be administered within 8 hours of the initial injury.^{2,14} The author suggests 2 protocols for administration of MPSS. Both require an initial loading dose of 30 mg/kg IV followed either by a decreased dose (15 mg/kg) in 2 hours and then 8 hours after the initial bolus or by a CRI of 5.4 mg/ kg/hr for 24 hours.²

Fluticasone
Fluticasone is the most commonly used inhaled steroid of those available.
Because they can be delivered directly to the site of inflammation with minimal systemic absorption, inhaled steroids are used to efficiently

treat inflammatory pulmonary diseases in dogs and cats (eg, asthma, chronic bronchitis, eosino-philic bronchopneumopathy). 15-17

Although it can take 1 to 2 weeks for inhaled steroids to decrease inflammation, clinicians commonly begin this course of therapy at the time of diagnosis, which is often in the emergency room.¹⁵ Most of these inflammatory pulmonary conditions are initially managed with oral steroids, but treatment is switched to inhaled steroids as soon as possible to avoid side effects. Pet owners should be shown how to use the inhaler and delivery chamber (preferably species-specific) while their pet is still in the clinic to provide them with multiple opportunities for supervised practice. Hands-on instruction can increase owner confidence in performing this technique at home and can hasten the transition from oral to inhaled steroids. Fluticasone is available through human pharmacies.

Conclusion

Corticosteroids comprise a broad group of pharmacologic agents with a choice of administration routes. In the critical care setting, these drugs treat conditions ranging from allergic reactions to acute soft tissue inflammation, autoimmune disease, asthma, spinal cord injury, and vasopressor nonresponsive hypotension in sepsis. Corticosteroids cause predictable dose-dependent side effects but remain a valuable drug class for use by critical care and emergency clinicians.

Continues **•**

Corticosteroids cause predictable dose-dependent side effects but remain a valuable drug class for use by critical care and emergency clinicians.

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

INDICATIONS: For use in dogs to prevent canine heartworm disease by eliminating the tissue stage of heartworm larvae (Dirofilaria immitis) for a month (30 days) after infection and for the treatment and control of ascarids (Toxocara canis, Toxascaris leonina) and hookworms (Ancylostoma caninum, Uncinaria stenocephala, Ancylostoma braziliense).

DOSAGE: HEARTGARD® Plus (ivermectin/pyrantel) should be administered orally at monthly intervals at the recommended minimum dose level of 6 mcg of ivermectin per kilogram (2.72 mcg/lb) and 5 mg of pyrantel (as pamoate salt) per kg (2.27 mg/lb) of body weight. The recommended dosing schedule for prevention of canine heartwork disease and for the treatment and control of ascarids and hookworms is as follows:

Dog Weight	Chewables Per Month	Ivermectin Content	Pyrantel Content	Color Coding On Foil Backing and Carton
Up to 25 lb	1	68 mcg	57 mg	Blue
26 to 50 lb	1	136 mcg	114 mg	Green
51 to 100 lb	1	272 mcg	227 mg	Brown

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 card with the remaining chewables to its 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

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 part of the dose is not lost or rejected. If it is suspected that any of the dose has been lost, redosing is recommended.

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.

When replacing another heartworm preventive product in a heartworm disease preventive program, the first dose of HEARTGARD Plus must be given within a month (30 days) of the last dose of the former medication.

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 once a month on or about the same day of the month. If treatment is delayed, whether by a few days or many, immediate treatment with HEARTGARD Plus and resumption of the recommended dosing regimen will minimize the opportunity for the development of adult heartworms.

Monthly treatment with HEARTGARD Plus also provides effective treatment and control of ascarids /T canis T leonina) and hookworms (A. caninum, U. stenocephala, A. braziliense). Clients should be advised of measures to be taken to prevent reinfection with intestinal parasites

EFFICACY: HEARTGARD Plus Chewables, given orally using the recommended dose and regimen, are effective against the tissue larval stage of D.immitis for a month (30 days) after infection and, as a result, p of the adult stage. HEARTGARD Plus Chewables are also effective against canine ascarids (T. canis, T. leonina) and hookworms (A. caninum, U. stenocephala, A. braziliense).

ACCEPTABILITY: In acceptability and field trials, HEARTGARD Plus was shown to be an acceptable oral dosage form that was consumed at first offering by the majority of dogs.

PRECAUTIONS: 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 at the recommended dose level, HEARTGARD Plus is not effective for microfilariae clearance. A mild 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 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.

Store between 68°F - 77°F (20°C - 25°C). Excursions between 59°F - 86°F (15°C - 30°C) are permitted. Protect product from light.

ADVERSE REACTIONS: In clinical field trials with 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, staggering, convulsions and hypersalivation

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 elevated dose levels (more than 16 times the target use level) than dogs of other breeds. At elevated doses, sensitive dogs showed adverse reactions which included mydriasis, depression, ataxia, tremors drooling, paresis, recumbency, excitability, stupor, coma and death. HEARTGARD demonstrated no signs of toxicity at 10 times the recommended dose (60 mcg/kg) in sensitive Collies. Results of these trials and bioequivalency studies, support 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, stud dogs and puppies aged 6 or more weeks. In clinical trials, many commonly used fle collars, dips, shampoos, anthelmintics, antibiotics, vaccines and steroid preparations have been administered with HEARTGARD Plus in a heartworm disease prevention program

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

HOW SUPPLIED: HEARTGARD Plus is available in three dosage strengths (See DOSAGE section) for dogs of different weights. Each strength comes in convenient cartons of 6 and 12 chewables.

For customer service, please contact Merial at 1-888-637-4251

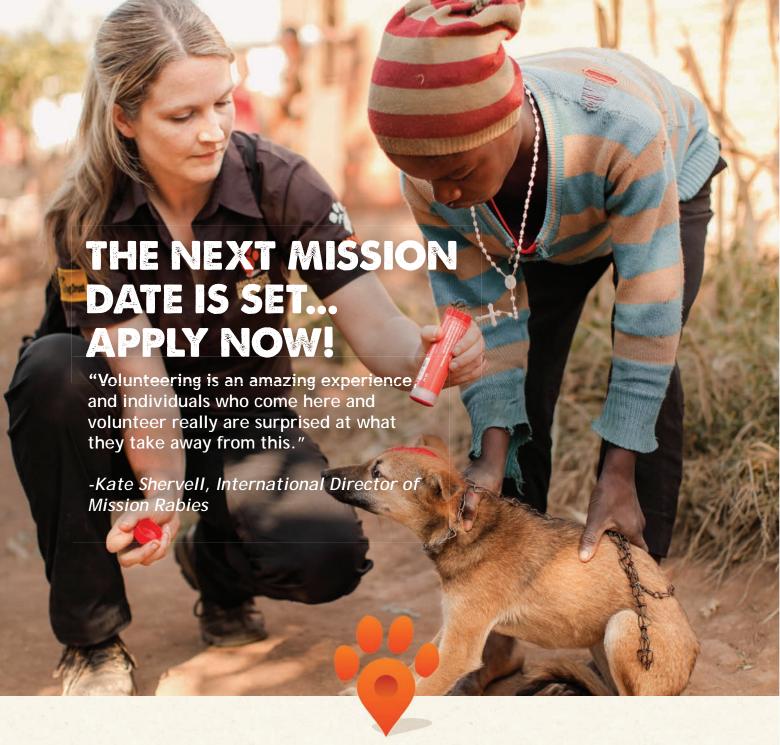


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IMPORTANT SAFETY INFORMATION: HEARTGARD® Plus (ivermectin/pyrantel) is well tolerated. All dogs should be tested for heartworm infection before starting a preventive program. Following the use of HEARTGARD Plus, digestive and neurological side effects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





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Credelio Receives FDA Approval

Elanco Animal Health (elanco.com) has announced that the US Food and Drug Administration has approved Credelio (credelio.com), a monthly oral treatment that protects dogs against fleas (Ctenocephalides felis) and ticks such as Lone Star tick (Amblyomma americanum), American dog tick (Dermacentor variabilis), blacklegged tick (Ixodes scapularis), and brown dog tick (Rhipicephalus sanguineus). Credelio contains the patented active ingredient lotilaner, which circulates in the dog's blood stream and targets the nervous system receptors of ticks and fleas. The initial onset of action provides rapid relief from existing ticks, and the sustained speed-of-kill throughout the dosing period provides protection from newly acquired ticks. When given with food, Credelio reaches peak blood levels within 2 hours of dosing.

Credelio is a small chewable tablet approved for dogs 8 weeks of age and older and weighing at least 4.4 lb. It has been proven to be well accepted by a broad range of breeds. Credelio will be available in 4 tablet strengths.—*Press Release* 1/2018

Merck Veterinary Manual App Now Free

The Merck Vet Manual (merckvetmanual.com) App has been updated and is now free, making digitally enhanced information readily available to more practitioners. The updated app is a comprehensive mobile resource for veterinarians, veterinary students, veterinary nurses and technicians, and other animal health professionals. Accessible on multiple handheld devices, the app provides authoritative guidelines for the diagnosis, treatment, and prevention of disorders and diseases in companion, exotic, laboratory, and food animals.

The mobile app offers:

- Numerous topics written by veterinary experts
- Photos, illustrations, and videos of disorders and diseases
- Clinical calculators
- Several reference guides and tables

All material resides on the mobile device after installation and therefore does not use data or require an internet connection. The app is available for download in the Apple App Store and the Google Play Store.—*Press Release* 1/2018

Dechra Announces New Dermatology Partnership

Dechra Veterinary Products (**dechra-us.com**) has signed an agreement with **Premune** (**premune.com**), a European animal health company, to add **Redonyl Ultra** to Dechra's topical dermatology portfolio. Redonyl Ultra is a patented and palatable veterinary nutraceutical that helps support healthy skin function and can be used as part of a multimodal approach to the management of atopic dermatitis in dogs. Redonyl Ultra contains palmitoylethanolamide, a naturally occurring biomodulator with activity against the mechanisms that contribute to inflammation and pain. Redonyl Ultra will be available in 2 soft chew strengths (100 mg and 200 mg) that is safe for dogs of all sizes. Redonyl Ultra will also carry the NASC Quality Seal from the National Animal Supplement Council. Dechra expects to have Redonyl Ultra available for sale to veterinarians in May.—*Press Release 1/2018*

SEND INFORMATION FOR PRACTICE HOTLINE TO editor@cliniciansbrief.com



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.

CREDELIO (lotilaner) is a beef-flavored, chewable tablet for oral administration to dogs and puppies according to their weight. Each chewable tablet is formulated to provide a minimum lotilaner dosage of 9 mg/lb (20 mg/kg).

Lotilaner has the chemical composition of 5-[(5S)-4,5-dihydro-5-(3,4,5-trichlorophenyl)-5-(trifluoromethyl)-3-isoxazolyl]-3-methyl-N-[2-oxo-2-[(2,2,2-trifluoroethyl)amino]ethyl]-2-thiophenecarboxamide.

Indications:

CREDELIO kills adult fleas and is indicated for the treatment 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 and Administration:

CREDELIO is given orally once a month, at the minimum dosage of 9 mg/lb (20 mg/kg).

Dosage Schedule:

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

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.

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.

Precaution

The safe use of CREDELIO in breeding, pregnant or lactating dogs has not been evaluated. Use with caution in dogs with a history of seizures (see **Adverse Reactions**).

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

Adverse Reaction (AR)	CREDELIO Group: Number (and Percent) of	Active Control Group: Number (and Percent) of
	Dogs with the AR (n=198)	Dogs with the AR (n=86)
Weight Loss	3 (1.5%)	2 (2.3%)
Elevated Blood Urea Nitrogen (BUN)	2 (1.0%)*	0 (0.0%)
Polyuria	2 (1.0%)*	0 (0.0%)
Diarrhea	2 (1 0%)	2 (2.3%)

*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/AnimalVeterinary/SafetyHealth.

Clinical Pharmacology:

Following oral administration of 43 mg/kg (approximately 1X the maximum labeled dose), peak lotilaner concentrations were achieved between 6 hours and 3 days in dogs 2 months of age and between 1 and 7 days in dogs 10 months of age. Dogs 2 months of age had a shorter elimination half-life (average of 9.6 days) than at 10 months of age (average of 28.4 days). Due to reduced drug bioavailability in the fasted state, CREDELIO must be administered with a meal or within 30 minutes after feeding.

Mode of Action:

Lotilaner is an ectoparasiticide belonging to the isoxazoline group. Lotilaner inhibits insect and acarine gamma-aminobutyric acid (GABA)-gated chloride channels. This inhibition blocks the transfer of chloride ions across cell membranes, which results in uncontrolled neuromuscular activity leading to death of insects and acarines. The selective toxicity of lotilaner between insects and acarines and mammals may be inferred by the differential sensitivity of the insects and acarines' GABA receptors versus mammalian GABA receptors.

Effectiveness:

In 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/pyodermatitis and pruritus as a direct result of eliminating fleas. 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

Palatability: In the U.S. field study, which included 567 doses administered to 198 dogs, 80.4% of dogs voluntarily consumed CREDELIO when offered by hand or in an empty bowl, an additional 13.6% consumed CREDELIO when offered with food, and 6.0% required placement of the chewable tablet in the back of the dog's mouth.

Animal Safety

ticks within four hours after administration.

In a margin of safety study, CREDELIO was administered orally to 24 (8 dogs/group) 8-week-old Beagle puppies at doses of 43 mg/kg, 129 mg/kg, and 215 mg/kg (approximately 1, 3, and 5X the maximum labeled dose, respectively) every 28 days for eight consecutive doses. The 8 dogs in the control group (0X) were untreated. There were no clinically-relevant, treatment-related effects on clinical observations, physical and neurological examinations, body weights, food consumption, electrocardiograms, clinical pathology (hematology, clinical chemistries, coagulation profiles and urinalysis), gross pathology, histopathology, or organ weights. Blood concentrations of lotilaner confirmed systemic exposure of all treated dogs, although the exposure was less than dose proportional at 5X.

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

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 or 6 chewable tablets.

NADA #141-494, Approved by the FDA

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Rev. date 11/2017 PA209456X 12266



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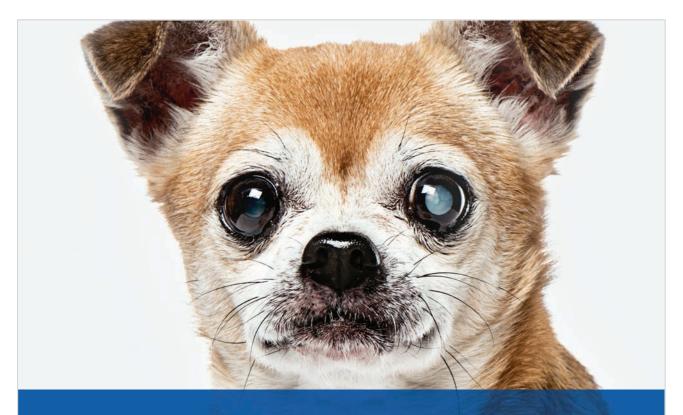
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CORNER

QUIZ YOURSELF

on this issue's features

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PROCEDURES PRO PAGE 14

Which portions of the intestinal tract are more amenable to performing stapled functional endto-end anastomosis based on their relative mobility?

- A. Duodenum and large intestine
- B. Duodenum and stomach
- C. Jejunum and large intestine
- D. Jejunum and ascending duodenum

TOP 5 PAGE 29

Bowenoid in situ carcinoma in cats is often a progression from viral plaque caused by:

- A. Feline pox virus
- B. Feline leukemia virus
- C. Feline herpesvirus 1
- D. Papillomavirus

CLINICAL VIEW PAGE 35

3 CLINICAL VIEW PAGE 33 Which of the following findings would *not* be observed on ophthalmologic examination of a patient with optic neuritis?

- A. Absent menace response
- B. Miotic pupils
- C. Swollen optic nerve
- D. Chorioretinitis

COMPARATIVE IMAGERY PAGE 70

Hematology analyzers that use impedance methodology can erroneously count large platelets as RBCs, resulting in a falsely decreased platelet count. This is particularly common in because their platelet and RBC sizes are similar.

- A. Cats B. Dogs
- C. Guinea pigs
- D. Horses

TOP 5 PAGE 75

In the absence of culture and susceptibility results for a patient with feline neutrophilic cholangitis, empiric therapy with 8 weeks is recommended.

- A. Tylosin
- B. Neomycin
- C. Metronidazole
- D. Amoxicillin-clavulanic acid

TOP 5 PAGE 85

Because cats are unable to convert prednisone to the active metabolite prednisolone:

- A. Prednisone is ineffective in cats
- B. Prednisone is contraindicated in cats
- C. Using lower dosages of prednisone than would be used with prednisolone is recommended
- D. Using higher dosages of prednisone than would be used with prednisolone is recommended

T: D 7: D 3: B 4: Y 2: D 6: D

POLLING

WE ASKED ...

Which anesthetic complication do you encounter most frequently?

YOU ANSWERED ...

Α.	Hypotension	31%
В.	Hypothermia	42%
C.	Abnormal heart rate	8%
D.	Hypoventilation	15%
E.	Difficult recovery	4%

THIS MONTH'S QUESTION ...

Which parasite have you never seen during microscopic evaluation?

- A. Cheyletiella spp (either C yasquri or C blakei)
- B. Capillaria plica
- C. Demodex gatoi
- D. Dirofilaria immitis microfilariae
- E. More than one of the above

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*Puppies and dogs 8 weeks of age and older and 4.4 pounds and greater.

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Credelio kills adult fleas and is indicated for the treatment 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.

IMPORTANT SAFETY INFORMATION

The safe use of Credelio in breeding, pregnant or lactating dogs has not been evaluated. Use with caution in dogs with a history of seizures. The most frequently reported adverse reactions are weight loss, elevated blood urea nitrogen, excessive urination, and diarrhea. See package insert for full safety information.

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

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A Staged Approach to Diagnosis and Management of Chronic Kidney Disease in Cats

A Roundtable Discussion Sponsored by Purina® Pro Plan® Veterinary Diets

DIAGNOSIS OF CHRONIC KIDNEY DISEASE

Dr. Laflamme: Chronic kidney disease (CKD) is a common diagnosis in middle-aged and older cats. Some estimates say more than 30% of cats 10 years or older are impacted with some degree of kidney disease. Knowing how common this condition is, should senior cats be routinely screened?

Dr. Churchill: I recommend a health screen for seniors, starting at age 7 or 8, that incorporates evaluation for renal disease. This screen includes a thorough medical and diet history, as well as a physical exam that includes kidney palpation, palpation of the colon and evaluation of body condition, muscle condition and body weight. A senior evaluation also includes a complete blood count (CBC), serum chemistry profile (including creatinine), a urinalysis, symmetric dimethylarginine (SDMA) and thyroid function. I reserve some of the urine sample to allow a culture or a urine protein creatinine ratio (UPC) if the urinalysis results indicate this follow-up is needed. I also measure the cat's blood pressure (BP).

Dr. Scherk: I start conducting what I call an annual "mature cat screening" at age 8. It includes a comprehensive physical examination and discussion regarding nutrition, along with performing a CBC, serum chemistry profile, urinalysis and BP. After 12 years of age, I increase the frequency to twice a year. It all depends on how the individual is doing; if they're ill, more frequent rechecks are needed.

Dr. Laflamme: Dr. Brown, you are a member of the International Renal Interest Society (IRIS), which focuses on post-diagnostic staging of CKD. How does IRIS outline its key diagnostic criteria and why are these important?

Dr. Brown: The IRIS group supports routine screening of middle-aged and senior cats, starting between 7 and 10 years of age. The idea of the staging system is to move toward individualized care; as CKD advances, patients need to be seen more frequently. By the time they reach stage 4 CKD, they should probably be seen at least every three months.

The diagnostic criteria forming the basis of the IRIS staging system is a fasting serum creatinine in a stable hydrated cat, augmented by appropriate additional tests. These should include a complete urinalysis, UPC, systolic arterial BP, body condition score (BCS) and, possibly, SDMA. While its use is still preliminary, we expect the IRIS guidelines to be updated as the veterinary profession gains experience using SDMA alongside creatinine.

Dr. Laflamme: How can practitioners improve their approach to diagnosing renal disease in cats?

Dr. Quimby: I think that one of the most important factors is to observe what's happening with the patient over time. I don't view diagnosis as a one-time lab test



"I think that one of the most important factors is to observe what's happening with the patient over time. I don't view diagnosis as a one-time lab test or event; a diagnosis of CKD comes from monitoring trends over time."

Dr. Jessica Quimby

or event; a diagnosis of CKD (see Table 1) comes from monitoring trends over time, whether it's changes in the creatinine level, urine specific gravity (USG) or the SDMA. My hope for practitioners is that by strengthening their clinical intuition about the onset of CKD, they can identify the disease earlier. I pay close attention to trends, which supports the value of regular screening for these patients, particularly as they become geriatric.

Dr. Churchill: I get a thorough history and find out why the cat is coming in. What's the back story? Are they just coming in for a wellness exam or is the cat really ill? Are they eating normally? Is their body weight and condition stable? Are they dehydrated?

Dr. Scherk: Related to that, a really easy way to assess hydration is to assess stool character—it doesn't lie. I ask the client to describe their cat's feces as hard pellets, moist logs, cow patties or colored water. Unless the cat has diarrhea, I can already tell if the cat is hydrated or dehydrated.

Dr. Brown: If it's in any way possible, I tell practitioners to get a urine sample and look at the specific gravity. If you evaluate an employee, you look at their work product, so why would a veterinarian evaluate the kidney and not look at its work product? If you want to evaluate

the kidney, you don't look in the ears—you obtain a urine sample coupled with a blood sample. It's essential. It will help to determine if a suspicious creatinine reading is renal, post-renal or pre-renal.

Dr. Quimby: I place a high importance on diagnostic imaging. I want a radiograph and ultrasound when azotemia is first diagnosed to get a better idea of what I might be missing in the kidney, particularly as it relates to stone disease or hydronephrosis that is related to a stricture or some other type of ureteral accident.

Dr. Laflamme: Would you comment on blood urea nitrogen (BUN)?

Dr. Quimby: I always look at it, but I rarely use it as a primary driver of my decision process, as we know that BUN is impacted by other factors. The USG might be trending downward. The SDMA might be elevated. So BUN is secondary for me when I'm evaluating the different parameters. I agree that it's really important to evaluate the patient's hydration and put it in the medical record. It gives me a more complete picture of what's going on, as well as how to interpret the creatinine and USG results.

Table 1. Diagnostic Testing and Evaluation for Feline CKD.

	Pre-diagnosis	Post-diagnosis
Physical evaluations		
Comprehensive physical examination and nutritional assessment	Annually after age 7 Semi-annually after age 12	Semi-annually*
Weight	At every visit	At every visit
Body Condition Score (BCS)	At every visit	At every visit
Muscle Condition Score (MCS)	At every visit	At every visit
Blood pressure (BP)	Annually after age 7 Semi-annually after age 12	At every visit

Laboratory tests		
Complete Blood Count (CBC)	Annually after age 7 Semi-annually after age 12	Semi-annually*
Serum Chemistry Panel	Annually after age 7 Semi-annually after age 12	Semi-annually*
Urinalysis	Annually after age 7 Semi-annually after age 12	Semi-annually*
Urine Protein: Creatinine** ratio (UPC)	Run if urinalysis shows increased protein	Semi-annually*
SDMA	In cats with low MCS	
Thyroid***	Annually after age 7	

^{*}Depends on stability of patient. If declining or in Stage 4, then increase frequency to every 3-4 months

^{**}Requires inactive sediment

^{***}Earlier screen if thyroid gland palpated or a history of weight loss occurs



"The more often practitioners perform BP evaluations, the better they get at doing them. It helps to start measuring

BP in both well cats and younger cats, when you're less concerned about the results."

Dr. Margie Scherk

Dr. Laflamme: Proteinuria is an important factor. When should UPC be measured?

Dr. Quimby: If proteinuria is present on the dipstick, I typically look at the urinalysis—including urine sediment—to determine if measuring UPC is appropriate to quantify proteinuria. This is necessary because we know the dipstick can be somewhat inaccurate, with both false-negative and false-positive results occurring. As a general rule, grossly bloody urine, or even 250-300 red blood cells per high-power field, could potentially impact the UPC. Just as with bacteriuria, these cells can represent inflammatory or infectious processes in the urinary tract that could confound test results.

It's important to note that there are big differences between CKD in the dog and cat. The majority of dogs have proteinuric kidney disease and are more likely to have glomerular kidney disease, as opposed to cats, which are more likely to have interstitial disease. True glomerular dysfunction in cats is fairly uncommon. My general impression is that low levels of tubular proteinuria tend to occur in later-stage cats as a sequela to their CKD as opposed to being the driving force.

Dr. Laflamme: Let's talk about blood pressure. How important is it to measure BP in cats with definitively diagnosed kidney disease?

Dr. Brown: Measuring BP in cats with CKD is extremely important. Between one-fourth and one-half of cats with CKD have systemic hypertension, which can add up to 15 percent of aged cats and up to 2 to 4 percent of all cats—and hypertension has important adverse consequences. A significant number of cats with unmanaged severe hypertension will have ocular abnormalities. Depression can also occur, but it can be difficult to know if the cat is depressed because of uremia or because of a hypertension-induced "headache," which is a common clinical finding in people with uncontrolled hypertension.

Dr. Scherk: The more often practitioners perform BP evaluations, the better they get at doing them. It helps to start measuring BP in both well cats and younger cats, when you're less concerned about the results.

Dr. Quimby: I agree—it's so important to look at the trends. If the cat typically is stressed when it comes to the hospital but has had normal BP evaluations over time, you can recognize what becomes an upward trend. As a tip, I recommend using headphones with the Doppler.

Dr. Laflamme: Let's talk about SDMA and explore the advantages or limitations you see to using this marker as a measure of kidney function.

Dr. Brown: Symmetric dimethylarginine is a by-product of somatic cell metabolism that's eliminated by renal filtration, so the concentration of SDMA in plasma reflects glomerular filtration rate (GFR). In the past, creatinine has been the hallmark for measuring adequacy of GFR because its elimination is by filtration in cats. A challenge with creatinine is that the rate of its production is dependent on skeletal muscle mass. As we all know, geriatric cats lose muscle mass, which causes creatinine production to fall. This means that "normal" ranges for older cats should be lower than for younger cats, but we don't yet have those ranges available to us.

I believe that we're very early in our use of SDMA. While it looks promising as a way to identify cats with chronic kidney disease earlier than creatinine does—especially as cats lose skeletal muscle mass—we don't yet know what variables there are to SDMA production.

Dr. Quimby: We desperately need biomarkers in order to better study chronic kidney disease and understand what happens with therapies, but no test is 100% right. I agree that we're early in understanding SDMA as a diagnostic and need to better understand its strengths and weaknesses. SDMA may be a way to further evaluate the IRIS stage and determine how to manage the disease at different points in time. Based on the SDMA, I may bump a patient from IRIS stage 2 up to stage 3, and with that comes heightened supportive care and monitoring. However, I do not want SDMA to become a substitute for not getting urine. I'm going to want to look at the creatinine, SDMA, USG and the urinalysis all together to make a decision about what's going on with the patient.

MEDICAL MANAGEMENT OF CHRONIC KIDNEY DISEASE

Dr. Laflamme: Amlodipine is an anti-hypertensive medication, while benazepril is an ACE inhibitor. How do these drugs work and when should they be used in the CKD cat?

Dr. Brown: Amlodipine is a calcium channel blocker that peripherally dilates the afferent arteriole in the cat. Meanwhile, benazepril indirectly but preferentially dilates the efferent arteriole, which is often thought to be a desirable effect.

Some papers suggest that amlodipine use carries some risks in other species, particularly people and rats. In the case of cats, however, I think it can substantially lower BP, thus obviating most of the risk to the kidney of dilating the afferent arteriole.

The IRIS guidelines suggest that these medications be introduced in the presence of persistent hypertension (systolic BP that exceeds 160 mmHg), which can occur in early stages—often in stage 2. It's important to ensure that patients are adequately hydrated before introducing ACE inhibitors to avoid precipitous drops in a patient's glomerular filtration rate.

Dr. Laflamme: What's your take on the use of phosphate binders in cats with CKD? When would you use them and when wouldn't you?

Dr. Churchill: I don't use them until I see a rise in serum phosphorus, which is usually at stage 3. I prefer to reduce phosphorus through diet first, then add phosphate binders if needed. I think adding phosphate binders on top of a diet that's not phosphorus-restricted has questionable efficacy.

Dr. Quimby: I would ask for someone to give me a tasty phosphate binder, because we struggle with this. If we put the phosphate binder in the food as opposed to trying diet first, we can be shooting ourselves in the foot, because phosphate binders can keep cats from meeting their caloric intake goals.

NUTRITIONAL MANAGEMENT OF CHRONIC KIDNEY DISEASE

Dr. Laflamme: That's a good segue to discussing diet and the role of nutrients (see Table 2) in managing CKD. Dietary protein restriction has been promoted for decades as an important component of management. Let's explore the basis for this long-standing recommendation.

Dr. Brown: Over the years, two separate rationales have been given for dietary protein restriction. The first, for cats in stages 3 and 4, is that some of the key uremic toxins are by-products of protein catabolism and that protein restriction would, therefore, reduce their production. The second rationale is the idea that protein restriction might slow the progression of kidney disease or prevent its onset. There is considerable doubt about this second idea—that dietary protein intake is a progression factor in dogs and cats.

There isn't any evidence in either species that the level of protein intake significantly impacts the rate of progression from IRIS stage 2 to 3 to 4. I don't think it's reasonable to recommend restriction of dietary protein as a treatment goal in early chronic kidney disease before the onset of clinical signs.

If we have a feline patient with low muscle condition score (MCS), low BCS and/or low lean body mass, it would seem that protein restriction would be an undesirable therapeutic maneuver. While there appears to be a valid argument that dietary protein restriction could reduce uremia in later stages, there's no data to indicate that restricting protein in earlier stages can slow the progression of disease in cats.

Dr. Laflamme: Were studies conducted on protein- and phosphorus-restricted diets or were the study diets specifically protein-restricted with phosphorus being maintained at normal levels?

Dr. Brown: The impacts of low protein and phosphorus were often not separated in studies. The data that reducing phosphate intake in cats is beneficial is overwhelming, and we're beginning to understand that it's important in uremia as well as progression. Thus, most—or all—of the benefits to renal diets seen in some studies could have been attributable to phosphorus restriction.



"There isn't any evidence in either species that the level of protein intake significantly impacts the rate of progression from IRIS stage 2 to 3 to 4. I don't think it's reasonable to recommend restriction of dietary protein as a treatment goal in early chronic kidney disease before the onset of clinical signs."

Pr. Scott Brown

Dr. Churchill: I agree. It is tricky because protein is often the source of phosphorus, and the two are lumped together. My biggest quandary is deciding how to manage cats in IRIS stage 2. There's such a range of variability in the clinical picture, and we need to make sure we're meeting the patient's minimum protein requirements. I'm much more resistant to feeding a traditional renal diet at this stage.

Dr. Laflamme: For what reasons might we want to restrict protein?

Dr. Quimby: I struggle because we don't have the studies we need, and the studies we have were done decades ago with diets that we're no longer feeding. Meanwhile, if you can't get the cat to eat, how can you evaluate what the right diet is, especially if it impacts intake? I get lost in the complexity.

Dr. Scherk: The role of body and muscle condition on longevity has been studied in cats with CKD as well as other conditions, such as cardiac disease and cancer. And we know that if a cat is losing muscle condition, the last thing we want to do is reduce their dietary protein.

Dr. Laflamme: So if you had a large group of cats and were going to feed half of them a lower-protein diet and half of them a higher-protein diet, would you expect to see a difference in muscle mass between those two groups of cats?

Dr. Churchill: I would expect the lower-protein ones to have a more rapid reduction in muscle condition as they age. It's largely clinical experience, but there are some studies that show protein requirements increase in cats as they age.

Dr. Scherk: Cats with CKD live a long time, and old cats need more protein. Rather than just focusing on the CKD, we need to focus on the whole cat.

Dr. Laflamme: Do we have evidence that phosphorus restriction is beneficial in cats or other species?

Dr. Brown: The evidence is strong that phosphorus restriction has a beneficial impact, as early as stage 2. I think we've got a lot more to learn about what that modification should look like, but there's clear evidence that phosphorus restriction can be beneficial. A low normal serum phosphorus has been identified as a harbinger of long survival.

There are proposed mechanisms for the benefit of phosphorus restriction, but we don't know exactly what is operating in cats with kidney disase. From the standpoint of a practicing veterinarian, elucidating the exact mechanism probably isn't critical. We know it helps!



"My biggest quandary is deciding how to manage cats in IRIS stage 2. There's such a range of variability in the clinical picture,

and we need to make sure we're meeting the patient's minimum protein requirements."

Dr. Julie Churchill

Dr. Laflamme: Is there any evidence to tell us what level of dietary phosphorus we should be targeting?

Dr. Churchill: It's not very academic. When selecting a diet, I set the protein as high and the phosphorus as low as I can. In terms of milligrams per kilocalorie, it is probably 100 milligrams or less—that's based on the renal diets currently out there. Right now, we just believe that less is best.

Dr. Laflamme: Let's talk about other nutrients that may be important in managing kidney disease, including omega-3 fatty acids and antioxidants. Why would those be beneficial?

Dr. Brown: An argument for using omega-3 in cats with chronic kidney disease could be their potential anti-inflammatory effects. In dog studies of chronic kidney disease, there was a clear benefit to omega-3 supplementation; in a study in cats, fairly high levels of supplementation tended to increase renal blood flow. At the time of the study, I thought the increase in renal blood flow from fish oil supplementation might potentially have a deleterious impact. Now my thinking has shifted on kidney disease in cats, with a focus on the role of tubulointerstitial hypoxia as a factor in progression. If intrarenal hypoxia turns out to be important in affected cats, then increasing renal blood flow could be beneficial.

Dr. Quimby: I am very interested in hypoxia and how oxidative stress might lead to potential damage. We've been studying telomere length and cellular senescence in CKD, and have demonstrated that telomeres are shorter in kidney disease. We cannot prove that telomeres are shorter in the elderly cat, but they are definitely shorter in cats with CKD, likely because of repeated replication and repair and oxidative stress.

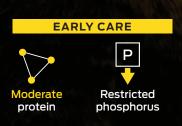
Dr. Churchill: Supplementing with antioxidants has become standard practice in diets for the senior pet. I think that because of the age of the population we're talking about (cats with CKD), antioxidants would be perceived to have potential benefit.

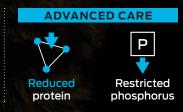


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