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**The Ehmer Sling in Canine  
Orthopedic Surgery**

**Panosteitis**

**Feline Plasma Cell Pododermatitis**

**Heart Murmurs in Dogs**

**Growling**

A Peer-Reviewed Journal • August 2015 • Volume 13 Number 8

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**Contraindications:** Dogs with known hypersensitivity to meloxicam should not receive Meloxidyl Oral Suspension. **Do not use Meloxidyl Oral Suspension in cats. Acute renal failure and death have been associated with the use of meloxicam in cats.**

**Warning:** Repeated use of meloxicam in cats has been associated with acute renal failure and death. Do not administer additional injectable or oral meloxicam to cats. See Contraindications, Warnings, and Precautions for detailed information.

**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. **For oral use in dogs only.**

As with any NSAID all dogs should undergo a thorough history and physical examination before the initiation of NSAID therapy. Appropriate laboratory testing to establish hematology and serum biochemical baseline data is recommended prior to and periodically during administration. Owner should be advised to observe their dog for signs of potential drug toxicity and be given a client information sheet about Meloxidyl Oral Suspension.

**Precautions:** The safe use of Meloxidyl Oral Suspension in dogs younger than 6 months of age, dogs used for breeding, or in pregnant or lactating dogs has not been evaluated. Meloxicam Oral Suspension is not recommended for use in dogs with bleeding disorders, as safety has not been established in dogs with these disorders. As a class, cyclo-oxygenase inhibitory NSAIDs may be associated with gastrointestinal, renal and hepatic toxicity. Sensitivity to drug-associated adverse events varies with the individual patient. Dogs that have experienced adverse reactions from one NSAID may experience adverse reactions from another NSAID. Patients at greatest risk for renal toxicity are those that are dehydrated, on concomitant diuretic therapy, or those with existing renal, cardiovascular, and/or hepatic dysfunction. Concurrent administration of potentially nephrotoxic drugs should be carefully approached. NSAIDs may inhibit the prostaglandins that maintain normal homeostatic function. Such antiprostaglandin effects may result in clinically significant disease in patients with underlying or pre-existing disease that has not been previously diagnosed. Since NSAIDs possess the potential to induce gastrointestinal ulcerations and/or perforations, concomitant use with other anti-inflammatory drugs, such as NSAIDs or corticosteroids, should be avoided. If additional pain medication is needed after administration of the total daily dose of Meloxidyl Oral Suspension, a non-NSAID or non-corticosteroid class of analgesia should be considered. The use of another NSAID is not recommended. Consider appropriate washout times when switching from corticosteroid use or from one NSAID to another in dogs. The use of concomitantly protein-bound drugs with Meloxidyl Oral Suspension has not been studied in dogs. Commonly used protein-bound drugs include cardiac, anticonvulsant and behavioral medications. The influence of concomitant drugs that may inhibit metabolism of Meloxidyl Oral Suspension has not been evaluated. Drug compatibility should be monitored in patients requiring adjunctive therapy.

**Adverse Reactions:** Field safety was evaluated in 306 dogs. Based on the results of two studies, GI abnormalities (vomiting, soft stools, diarrhea, and inappetence) were the most common adverse reactions associated with the administration of meloxicam. The following table lists adverse reactions and the numbers of dogs that experienced them during the studies. Dogs may have experienced more than one episode of the adverse reaction during the study.

In foreign suspected adverse drug reaction (SADR) reporting over a 9 year period, incidences of adverse reactions related to meloxicam administration included: auto-immune hemolytic anemia (1 dog), thrombocytopenia (1 dog), polyarthritis (1 dog), nursing puppy lethargy (1 dog), and pyoderma (1 dog).

Adverse Reactions Observed During Two Field Studies		
Clinical Observation	Meloxicam (n=157)	Placebo (n=149)
Vomiting	49	48
Diarrhea/Soft Stool	19	11
Bloody Stool	1	0
Inappetence	5	1
Bleeding Gums After Dental Procedure	1	0
Lethargy/Swollen Campus	1	0
Erythema	1	0

#### Post-Approval Experience: (Rev 2010)

The following adverse events are based on post-approval adverse drug experience reporting. Not all adverse reactions are reported to FDA/CVM. It is not always possible to reliably estimate the adverse event frequency or establish a causal relationship to product exposure using these data. The following adverse events are listed in decreasing order of frequency by body system.

**Gastrointestinal:** vomiting, anorexia, diarrhea, melena, gastrointestinal ulceration

**Urinary:** azotemia, elevated creatinine, renal failure

**Neurological/Behavioral:** lethargy, depression

**Hepatic:** elevated liver enzymes

**Dermatologic:** pruritus

Death has been reported as an outcome of the adverse events listed above. **Acute renal failure and death have been associated with use of meloxicam in cats.**

**Effectiveness:** The effectiveness of meloxicam was demonstrated in two field studies involving a total of 227 dogs representing various breeds, between six months and sixteen years of age, all diagnosed with osteoarthritis. Both of the placebo-controlled, masked studies were conducted for 14 days. All dogs received 0.2 mg/kg on day 1. All dogs were maintained on 0.1 mg/kg oral meloxicam from days 2 through 14 of both studies. Parameters evaluated by veterinarians included lameness, weight-bearing, pain on palpation, and overall improvement. Parameters assessed by owners included mobility, ability to rise, limping, and overall improvement. In the first field study (n=109), dogs showed clinical improvement with statistical significance after 14 days of meloxicam treatment for all parameters. In the second field study (n=48), dogs receiving meloxicam showed a clinical improvement after 14 days of therapy for all parameters; however, statistical significance was demonstrated only for the overall investigator evaluation on day 7, and for the owner evaluation on day 14.

**How Supplied:** Meloxidyl® 1.5 mg/mL Oral Suspension: 10, 32, 100 and 200 mL bottles with small and large dosing syringes.

**Storage:** Store at controlled room temperature 68-77°F (20-25°C).

**Manufactured for:** Ceva Santé Animale, Libourne, France

**Marketed by:** Ceva Animal Health, LLC, Lenexa, KS 66215

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DO NOT USE MELOXIDYL ORAL SUSPENSION IN CATS. Acute renal failure and death have been associated with the use of meloxicam in cats. Dogs with known hypersensitivity to meloxicam or other NSAIDs should not receive Meloxidyl Oral Suspension. Meloxidyl Oral Suspension is not recommended for use in dogs with bleeding disorders. If vomiting, diarrhea, decreased appetite or other signs of illness are seen, discontinue treatment immediately.

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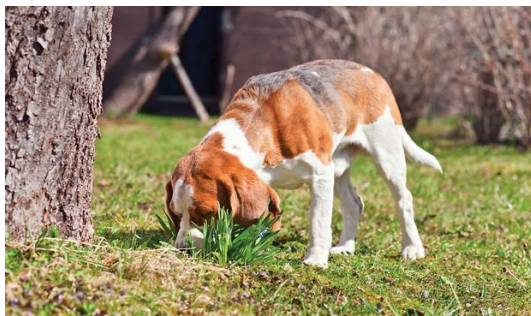
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# Feline Plasma Cell Pododermatitis

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Animal Dermatology Center  
Studio City, California

**Amanda Zetwo, DVM**

VCA Central  
Upland, California

Feline plasma cell pododermatitis (FPP) most commonly causes swelling of the metacarpal pads, metatarsal pads, or digital pads. These signs are followed by hyperkeratosis and ulcerations that may bleed. The majority of cases are diagnosed late in the disease process.

The cause of FPP is unknown, but immune hyperreactivity is suspected based on positive response to immunomodulatory therapy.<sup>1,2</sup> Food hypersensitivity has been associated with FPP in some patients, and improvement may be noted with diet trials.\*

Seasonal waxing and waning—particularly in spring and summer—have been described, but current studies have not identified an infectious causative agent.<sup>3</sup>

One study noted that more than half of cats with FPP were FIV-positive; however, viral and/or retroviral association is often not seen.<sup>2</sup> There is no reported sex, breed, or age predilection. Presentation varies from a single affected footpad to multiple affected pads on multiple paws. Footpads may be painful, and peripheral lymphadenopathy may be present.

Plasmacytic stomatitis, immune-mediated glomerulonephritis, and renal amyloidosis have been concurrently reported in rare cases.<sup>1</sup>

## Diagnosis

Gross appearance of FPP (Figures 1-3) is generally diagnostic. Cytologic

examination of affected pads shows plasma cells with or without lymphocytes and neutrophils.

Hypergammaglobulinemia is a frequent finding. Definitive diagnosis requires examination of a biopsy specimen of the affected pad. Early lesions demonstrate superficial and deep perivascular dermatitis with plasma cells predominating and possibly containing Russell bodies, which are large eosinophilic immunoglobulin-containing inclusions.

The main differential diagnoses include eosinophilic granuloma, pemphigus foliaceus, vasculitis, and acetaminophen toxicosis.

## Treatment

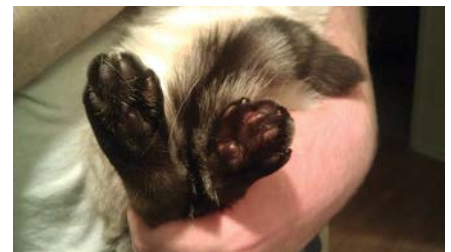
Response can be varied. Some cases resolve spontaneously; others may require courses of treatment with either corticosteroids or cyclosporine. Life-long therapy may be necessary.

In one study,<sup>2</sup> doxycycline was reported to produce partial or complete clinical remission in more than half of the cases. This remission is likely caused by immunomodulatory effects, such as inhibition of neutrophil chemotaxis and suppression of phagocytosis and lymphocyte proliferation.

Of note, chronic use of an antibiotic for a reason other than its antimicrobial effect is inconsistent with the principles of prudent antibiotic use. ■ **cb**



**1** Swelling of the digits on both thoracic limbs. Digit 3 of left limb is particularly affected. Pain and lameness were observed.



**2** Swelling and erythema affecting the left rear footpads. The right foot appears unaffected.



**3** The metatarsal pad is swollen and excessively soft, with surface white striae characteristic of plasma cell pododermatitis.

## References

1. Dias Pereira P, Faustino AM. Feline plasma cell pododermatitis: A study of 8 cases. *Vet Dermatol.* 2003;14(6):333-337.
2. Drolet R, Bernard J. Plasma cell pododermatitis in a cat. *Can Vet J.* 1984;25(12):448-449.
3. Taylor JE, Schmeitzel, LP. Plasma cell pododermatitis with chronic footpad hemorrhage in two cats. *JAVMA.* 1990;197(3):375-377.

FPP = feline plasma cell pododermatitis

\*Based on anecdotal clinical experience.



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# Panosteitis

Mary Sarah Bergh, DVM, MS, DACVS, DACVSMR

Iowa State University

Panosteitis is a disease of the medullary bone that begins with adipocyte degeneration, intramembranous ossification, and bony remodeling that results in medullary fibrosis and periosteal/endosteal new bone formation; it should be considered a differential for any lameness in a young dog.

## Clinical Signs

Panosteitis usually affects rapidly growing large- and giant-breed dogs, typically between 5 and 12 months of age, although it has been reported in dogs as old as 5 years of age.<sup>1,2</sup> Some studies have found that German shepherd dogs and male dogs are overrepresented.<sup>1-3</sup>

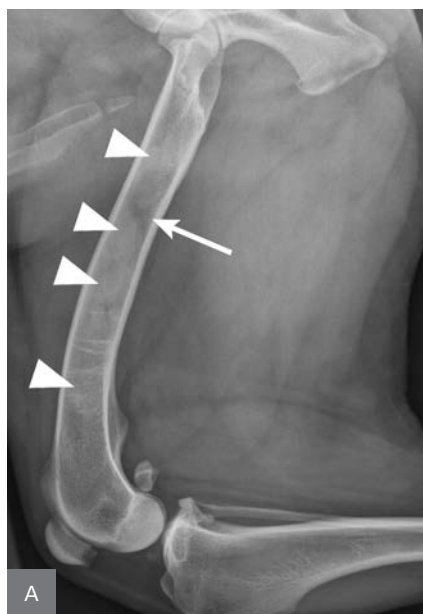
Panosteitis causes an acute onset of lameness unaffected by rest or activity. Lethargy and inappetence can be seen for a few days at onset. More than 1 bone may be affected at a time. Clinical signs can commonly regress spontaneously in 1 limb and then occur in other limbs, causing a characteristic shifting leg lameness.

## Diagnosis

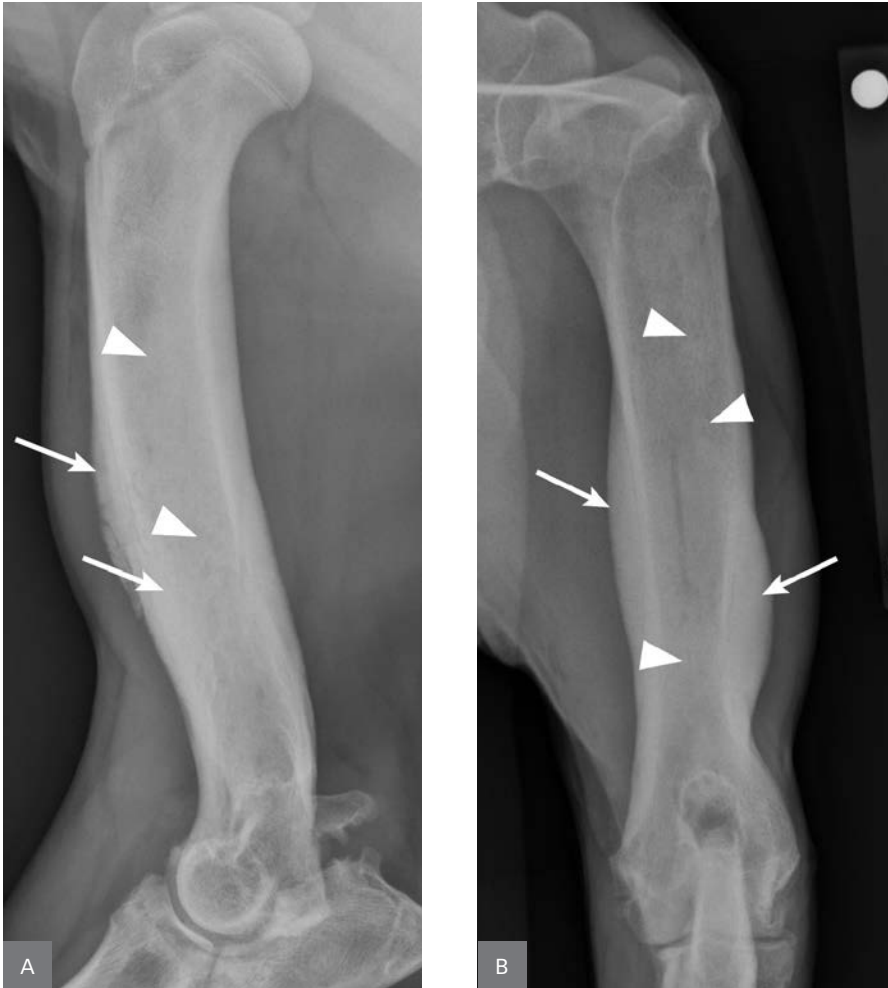
A thorough physical and orthopedic examination is important, as other orthopedic diseases (eg, osteochondrosis, hypertrophic osteodystrophy) may be similar to signs of panosteitis and, in some cases, occur concurrently.

Pain on direct palpation of the diaphysis of long bones is characteristic of panosteitis. The ulna is most commonly affected, followed in frequency by the radius and humerus.<sup>1</sup> Radiographs should be obtained to confirm diagnosis and rule out other pathologies.

Radiographic signs of panosteitis frequently lag days to weeks behind clinical signs.<sup>1,3</sup> The earliest radiographic sign of panosteitis is a decrease in opacity around the nutrient foramen. Later signs include an increase in mineral opacity within the medullary canal of long bones and loss of the normal trabecular bone pattern (**Figure 1**). Smooth periosteal and endosteal new



1 Lateral radiographic projections of the femur (A) and ulna (B) in dogs with early signs of panosteitis. Note the radiolucency around the nutrient foramen (arrows) and increased opacity within the medullary canal (arrowheads) in both cases.



**2** Lateral (A) and craniocaudal (B) radiographic projections of the humerus of an 11.5-month-old German shepherd dog with advanced panosteitis. Note the increase in mineral opacity within the medullary canal (arrowheads) as well as smooth periosteal and endosteal new bone formation (arrows). This dog also has an ununited anconeal process.

**For each recurrence of clinical signs, panosteitis should be confirmed through clinical examination and radiography to rule out other orthopedic causes.**

bone may also be seen in more severe cases (Figure 2). Radiographs of the affected limb may be compared with those of the contralateral limb to assist in diagnosis. Nuclear scintigraphy may assist in diagnosis in cases in which radiographic changes have not yet developed.<sup>4</sup>

### Treatment

Although the underlying pathogenesis of the condition is unknown, panosteitis is a self-limiting disease and resolves on its own. During episodes of pain and lameness, analgesia may be provided with

NSAIDs, tramadol, narcotic analgesics, or gabapentin.

### Prognosis

Episodes of pain and lameness from panosteitis last 2 to 5 weeks in each affected bone. It may recur until the patient is about 2 years of age, after which there are typically no long-term sequelae.<sup>1,3</sup> For each recurrence of clinical signs, panosteitis should be confirmed through clinical examination and radiography to rule out other orthopedic causes. ■ **cb**

### References

1. Böhning RH Jr, Suter PF, Hohn RB, Marshall J. Clinical and radiologic survey of canine panosteitis. *JAVMA*. 1970;156(7):870-883.
2. LaFond E, Breur GJ, Austin CC. Breed susceptibility for developmental orthopedic diseases in dogs. *JAAHA*. 2002;38(5):467-477.
3. Barrett RB, Schall WD, Lewis RE. Clinical and radiographic features of canine eosinophilic panosteitis. *JAAHA*. 1968;4:94-104.
4. Schwarz T, Johnson VS, Voute L, Sullivan M. Bone scintigraphy in the investigation of occult lameness in the dog. *J Small Anim Pract*. 2004;45(5):232-237.



**MARY SARAH BERGH, DVM, MS, DACVS, DACVSMR**, is associate professor of orthopedic surgery and director of the Canine Rehabilitation Center at Iowa State University. Her clinical and research interests include rehabilitation therapy, joint replacement, arthroscopy, treatments for cranial cruciate ligament disease, and sporting injuries. A graduate of University of Wisconsin, Dr. Bergh completed an internship at University of Pennsylvania and a residency in small animal surgery at The Ohio State University. **CLINICAL VIEW PAGE 10**



**LUIZ BOLFER, DVM**, is cardiology resident and PhD student at University of Florida, where he studies veterinary clinical sciences with an emphasis in cardiac gene therapy. His research interests include extra-corporeal blood purification therapy, myocardium dysfunction and failure, and cardiac regenerative medicine. A graduate of Universidade Tuiuti do Paraná, Dr. Bolfer completed a small animal medicine and surgery internship at University of Illinois and a residency in emergency and critical care at University of Florida. **CUTTING EDGE PAGE 35**



**AMARA ESTRADA, DVM, DACVIM (Cardiology)**, is associate professor and service chief of the cardiology department in the small animal hospital at University of Florida. Dr. Estrada's research interests include electrophysiology, pacing therapy, complex arrhythmias, cardiac interventional therapy, and cardiac regenerative medicine. Dr. Estrada graduated from University of Florida and completed a cardiology residency at Cornell University. **CUTTING EDGE PAGE 35**



**LORE I. HAUG, DVM, MS, DACVB**, works in a private referral, behavior-only practice in Sugar Land, Texas. Dr. Haug, who is certified through the International Association of Animal Behavior Consultants, speaks routinely to veterinary groups and animal trainers across the country. Author of numerous articles and book chapters, Dr. Haug is co-author of *Decoding Your Dog* by the American College of Veterinary Behaviorists. **APPLIED BEHAVIOR PAGE 15**

continues on page 84

## Loxicom® (meloxicam)

### 1.5 mg/mL Oral Suspension

Non-steroidal anti-inflammatory drug for oral use in dogs only

**Warning:** Repeated use of meloxicam in cats has been associated with acute renal failure and death. Do not administer additional injectable or oral meloxicam to cats. See Contraindications, Warnings, and Precautions for detailed information.

**Brief Summary:** Before using Loxicom Oral Suspension, consult the product insert, a summary of which follows.

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

**Description:** Meloxicam is a non-steroidal anti-inflammatory drug (NSAID) of the oxicam class.

**Indications:** Loxicom Oral Suspension is indicated for the control of pain and inflammation associated with osteoarthritis in dogs.

**Contraindications:** Dogs with known hypersensitivity to meloxicam should not receive Loxicom Oral Suspension.

**Do not use Loxicom Oral Suspension in cats. Acute renal failure and death have been associated with the use of meloxicam in cats.**

**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. **For oral use in dogs only.** As with any NSAID all dogs should undergo a thorough history and physical examination before the initiation of NSAID therapy. Appropriate laboratory testing to establish hematological and serum biochemical baseline data is recommended prior to and periodically during administration. To report suspected adverse reactions, to obtain a Material Safety Data Sheet, or for technical assistance, call Norbrook at 1-866-591-5777.

**Precautions:** The safe use of Loxicom Oral Suspension in dogs younger than 6 months of age, dogs used for breeding, or in

pregnant or lactating dogs has not been evaluated. As a class, cyclo-oxygenase inhibitory NSAIDs may be associated with gastrointestinal, renal and hepatic toxicity. Sensitivity to drug-associated adverse events varies with the individual patient. Patients at greatest risk for renal toxicity are those that are dehydrated, on concomitant diuretic therapy, or those with existing renal, cardiovascular, and/or hepatic dysfunction. Concurrent administration of potentially nephrotoxic drugs should be carefully approached. NSAIDs may inhibit the prostaglandins that maintain normal homeostatic function. Such anti-prostaglandin effects may result in clinically significant disease in patients with underlying or pre-existing disease that has not been previously diagnosed. Since NSAIDs possess the potential to induce gastrointestinal ulcerations and/or perforations, concomitant use with other anti-inflammatory drugs, such as NSAIDs or corticosteroids, should be avoided or closely monitored. The use of concomitantly protein-bound drugs with Loxicom Oral Suspension has not been studied in dogs. Commonly used protein-bound drugs include cardiac, anticonvulsant and behavioral medications. The influence of concomitant drugs that may inhibit metabolism of Loxicom Oral Suspension has not been evaluated. Drug compatibility should be monitored in patients requiring adjunctive therapy.

**Adverse Reactions:** Field safety was evaluated in 306 dogs. Based on the results of two studies, GI abnormalities (vomiting, soft stools, diarrhea, and inappetence) were the most common adverse reactions associated with the administration of meloxicam. Of the dogs that took meloxicam (n=157), forty experienced vomiting, nineteen experienced diarrhea/soft stool, five experienced inappetence, and one each experienced bloody stool, bleeding gums after dental procedure, lethargy/swollen carpus, and epiphora. Of the dogs that took the placebo (n=149), twenty-three experienced vomiting, eleven experienced diarrhea/soft stool, and one experienced inappetence. In foreign suspected adverse drug reaction (SADR) reporting over a 9 year period, incidences of adverse reactions related to meloxicam administration included: auto-immune hemolytic anemia (1 dog), thrombocytopenia (1 dog), polyarthritis (1 dog), nursing puppy lethargy (1 dog), and pyoderma (1 dog).

**Effectiveness:** The effectiveness of meloxicam was demonstrated in two field studies involving a total of 277 dogs representing various breeds, between six months and sixteen years of age, all diagnosed with osteoarthritis. Both of the placebo-controlled, masked studies were conducted for 14 days. All dogs received 0.2 mg/kg on day 1. All dogs were maintained on 0.1 mg/kg oral meloxicam from days 2 through 14 of both studies. Parameters evaluated by veterinarians included lameness, weight-bearing, pain on palpation, and overall improvement. Parameters assessed by owners included mobility, ability to rise, limping, and overall improvement. In the first field study (n=109), dogs showed clinical improvement with statistical significance after 14 days of meloxicam treatment for all parameters. In the second field study (n=48), dogs receiving meloxicam showed a clinical improvement after 14 days of therapy for all parameters; however, statistical significance was demonstrated only for the overall investigator evaluation on day 7, and for the owner evaluation on day 14.

**How Supplied:** Loxicom Oral Suspension 1.5 mg/mL: 10, 32 and 100 mL bottles with small and large dosing syringes.

**Storage:** Store at controlled room temperature 68-77°F (20-25°C). Excursions permitted between 59°F and 86°F (15°C and 30°C). Brief exposure to temperature up to 104°F (40°C) may be tolerated provided the mean kinetic temperature does not exceed 77°F (25°C); however such exposure should be minimized.

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\*Source: Bayer Veterinary Care Usage Study III, 2013

Observe label directions. **Do not use Loxicom Oral Suspension in cats. Acute renal failure and death have been associated with the use of meloxicam in cats.** As with any medication, side effects may occur. These are usually mild, but may be serious. The most common side effects reported in field studies were vomiting, soft stool/diarrhea and decreased appetite. If side effects occur, discontinue treatment immediately and consult a veterinarian. Dogs should be evaluated for pre-existing medical conditions prior to treatment and monitored during therapy. See product labeling for full product information.

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See page 12 for product information summary.

  
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# Growling in Dogs

**Lore I. Haug, DVM, MS, DACVB**

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A growl is a guttural vocalization most commonly emitted by an animal during agonistic interactions—situations of threat or defense.<sup>1,2</sup> Dogs growl at humans and other animals in various circumstances; the following focuses on growling directed toward humans. However, the purpose of growling and principles for addressing it are the same regardless of the intended target.

## Why Do Dogs Growl?

Growling is a true communication signal, the purpose of which is to influence the behavior of the receiver. Growling in agonistic situations is a distance-increasing signal in which the goal is to get the receiver to stop its advance or interaction and withdraw.

Growling can also occur in the context of play. In this case, play metasignals occur to let the receiver know that the growling is nonthreatening. (Metasignals, such as a play bow, are essentially modifiers—gestures or actions a dog takes that put the subsequent behaviors in proper context so the receiver knows how to respond.) Dogs may also growl as a means of seeking attention. This is a learned behavior that often originates from play. Similar to play, other body signals associated with threat or defense will be absent during attention-seeking growling.

Dogs also may growl when approached by unfamiliar people or dogs, during handling or maintenance procedures (eg, nail trims, vaccinations), when the dog is verbally or physically reprimanded, or when someone tries to take away a high-value possession.

Of note, growling is not a diagnosis; it is a clinical sign. Like any other clinical sign, growling signals an underlying problem that needs to be addressed (see **When Growling Is Not Normal**, next page).

## When Is Growling Good?

Growling is one stage of threat intensity. A dog's early warning may include signs of fear or avoidance, such as turning the head away, licking the lips, pinching the ears back, cowering, and/or freezing. As the intensity of the threat—and therefore the dog's response—escalates, this may intensify to growling, snarling, snapping, and biting.

In a perfect world, these behaviors occur on a distinct continuum—that is, a protracted warning phase before escalating to biting. In reality, however, threat behaviors may occur in a less predictable sequence, simultaneously, or with some behaviors entirely absent. Dogs may show extremely brief warning sequences giving the impression that they bite without warning. This may occur in part because warning signals such as growling have been modified through learning (eg, punishment, reinforcement).



**When, if ever, is growling acceptable? When should it be cause for concern?**

continues

There is some suggestion that suppression of growling can occur without accompanying suppression of fear or biting. In other words, a dog can be conditioned to skip growling as a warning and go directly to biting. This is most likely to occur in situations where dogs are punished when they growl but someone continues to threaten or antagonize the dog. For example, if a dog is punished for growling at an approaching visitor, the owner may be successful in eliminating the dog's growl. The dog may sit quietly without growling while the visitor approaches, but the dog is still fearful. (The dog is likely still displaying other subtle or clear signs of discomfort or anxiety, but these are frequently missed by owners and visitors.) If the visitor reaches toward the dog, it may still bite because suppression of the growling did not address the dog's underlying fear. Absence of growling and lack of recognition among owners of other signs of fear can create a dangerous situation for both humans and dogs.

Although people may not like the fact that a dog feels the need to growl, the behavior does serve as a warning of its discomfort before the dog resorts to the more dangerous behavior of biting.

### How Do We Handle or Treat Growling?

As with any other clinical sign, treating the underlying cause of growling is important. When a dog scratches, we discover, then treat, the underlying cause of the pruritus. Similarly, we do not focus on treating growling directly. When a dog growls, it is telling us there is a problem that, if not addressed, may escalate in the future to something more intense (eg, biting).

The first step is to identify the immediate antecedent for the growling—the specific action that occurs immediately before growling begins. The second step is to determine the function growling serves for the dog—the when, where, and toward whom (see **Important History Questions**).

The most immediate response that occurs after the growl likely has the most impact on reinforcing growling. For example, consider a dog resting on the couch: the owner approaches and tells the dog to get off. Because the owner has never systematically taught the dog the off command, the dog is unclear about what it

#### When Growling Is *Not* Normal

Growling directed at an individual is a normal behavior that serves a functional purpose. With the exception of play, growling that occurs in the absence of a receiver (eg, the animal is alone in a room) suggests an underlying organic pathology such as neurologic disease, and the animal should be evaluated accordingly.

#### Important History Questions

- Is the growling directed toward humans, other animals, or both?
- Is it directed at any particular individual?
- Where does growling occur—outside, inside, in certain rooms of the house, when the dog is in a specific location?
- When does the growling occur—when the dog is approached, for example, or when a high-value resource, such as a bone, is present?
- What consequence does the growling obtain? If the dog turns its head away and growls when someone walks near the dog while it is on the bed, growling serves to keep people from approaching while the dog is resting.

should do and remains on the couch. Now the owner points at the dog, leans forward, and tells the dog more firmly to get off. The dog turns its head away slightly but remains on the couch. The owner then reaches to pull on the dog's collar and the dog growls. The owner pulls his or her hand back and walks away. The dog now gets to remain on the couch, but the most immediate reinforcer for the dog was the owner removing his or her hand from the dog's collar and withdrawing the threatening postures. Whereas the owner thinks the dog is growling to stay on the couch, the dog may actually be growling to get the owner to stop threatening it.


This distinction is important in helping owners formulate solutions because the final step is to devise a behavior modification program to treat the underlying problem. In this example, the approach for growling is to systematically teach the dog to get off the couch on cue using positive reinforcement, so the owner does not have to resort to threatening the dog and pulling on its collar.

#### Conclusion

Growling is a valuable warning sign that allows us to decipher a dog's tolerance level for a certain situation or action without direct injury. Growling should be addressed by determining and treating the underlying reason for the animal's behavior (eg, fear or anxiety), not by punishing or correcting the growling itself. ■ **cb**

#### References

1. Beaver BV. *Canine Behavior: A Guide for Veterinarians*. Philadelphia, PA: WB Saunders;1999:109.
2. Serpell J, ed. *The Domestic Dog: Its Evolution, Behaviour and Interactions with People*. Cambridge, UK: Cambridge University Press;1996:117.



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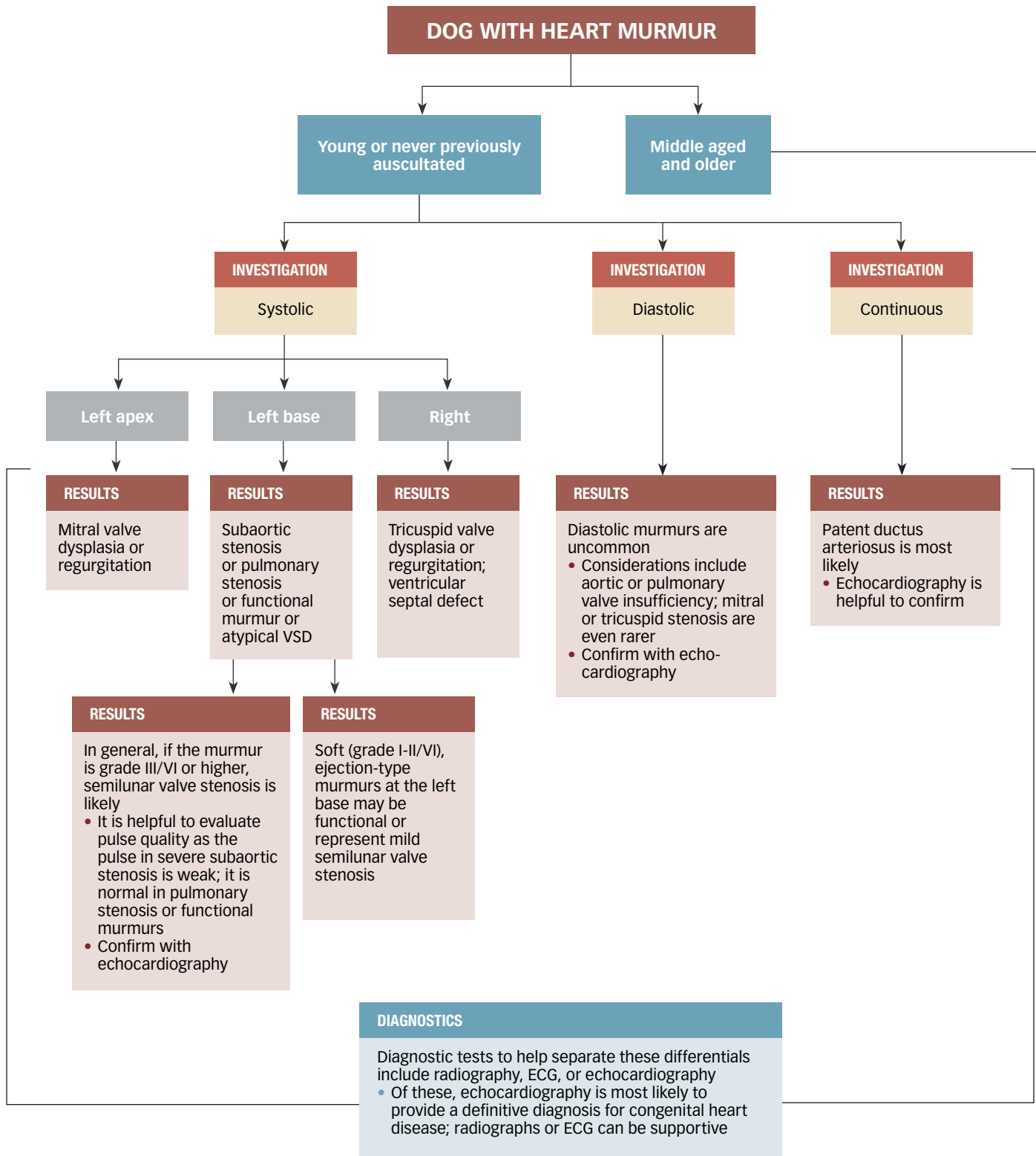
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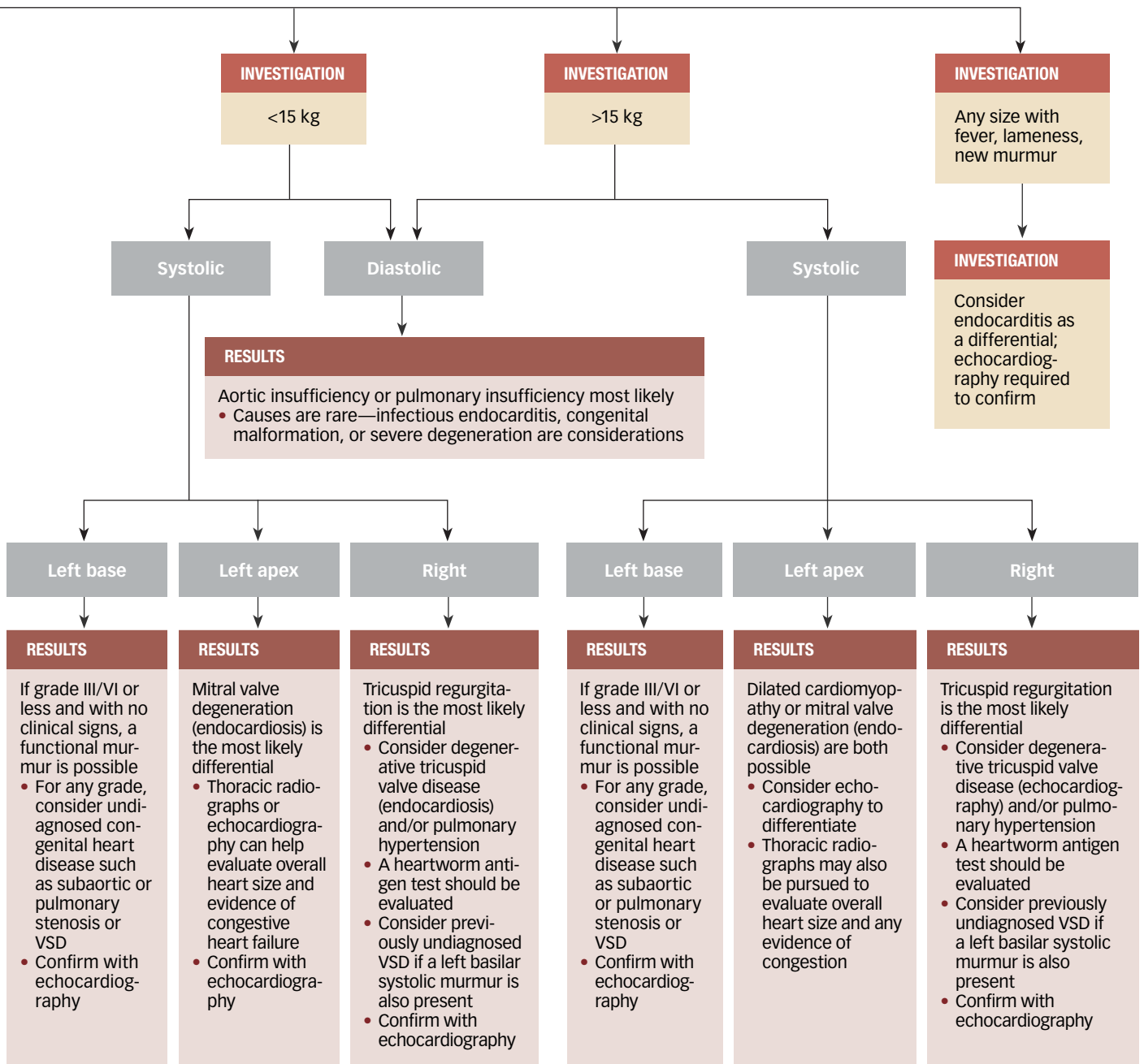
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# Heart Murmurs in Dogs

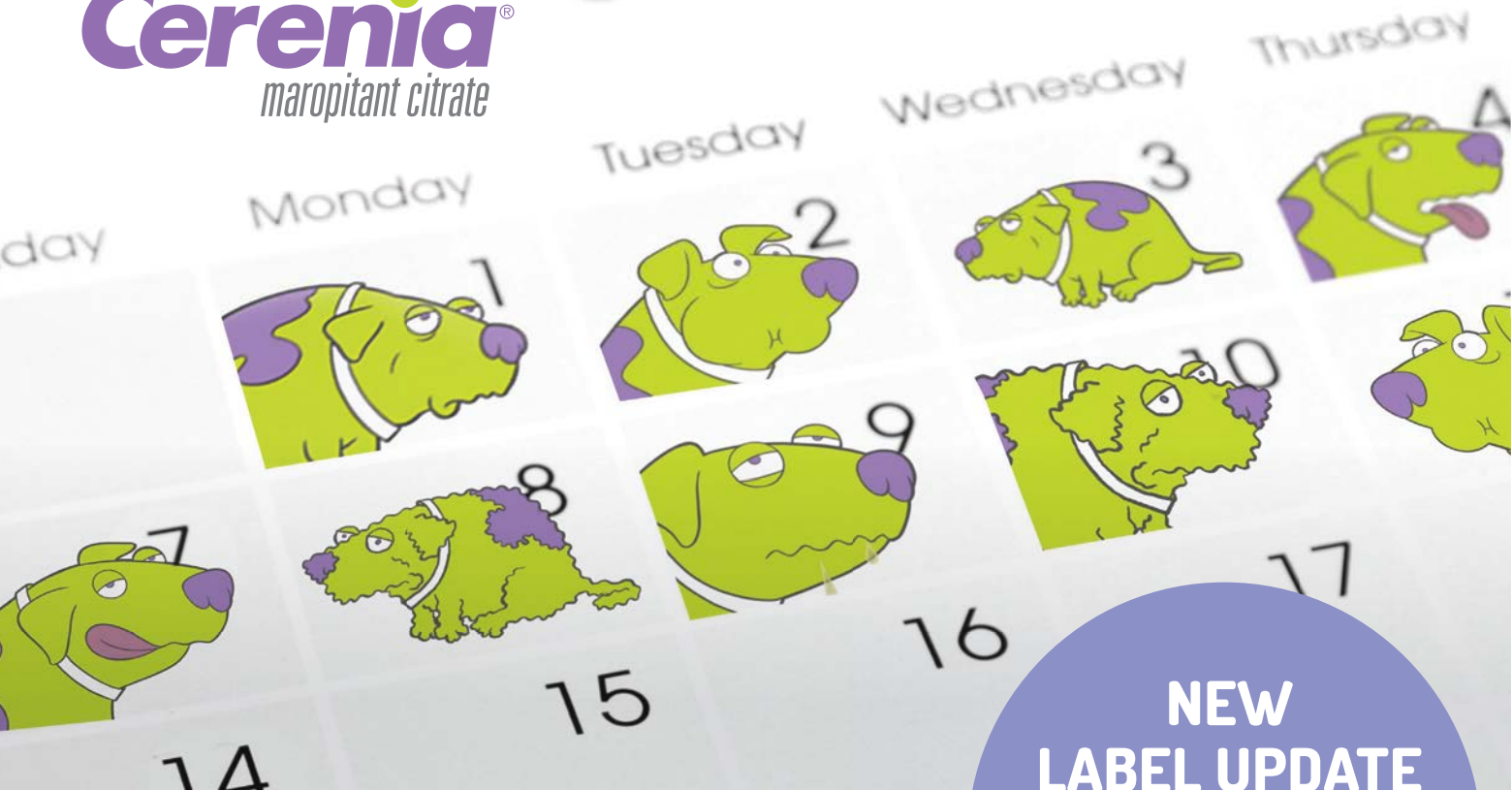




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### IMPORTANT SAFETY INFORMATION:

Use CERENIA Tablets until resolution of acute vomiting in dogs 7 months and older. Safe use has not been evaluated in cats and dogs with gastrointestinal obstruction, or those that have ingested toxins. Use with caution in dogs with hepatic dysfunction. In people, topical exposure may elicit localized allergic skin reactions, and repeated or prolonged exposure may lead to skin sensitization. See Brief Summary of Prescribing Information on page 21.

## Brief Summary of Prescribing Information

# Cerenia<sup>®</sup>

(maropitant citrate)  
Tablets

### Antiemetic

### For oral use in dogs only

#### CAUTION:

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

#### INDICATIONS:

CERENIA (maropitant citrate) Tablets are indicated for the prevention of acute vomiting and the prevention of vomiting due to motion sickness in dogs.

#### DOSE AND ADMINISTRATION:

##### For Prevention of Acute Vomiting

**For Prevention of Acute Vomiting in dogs 2-7 months of age:** Administer CERENIA Tablets orally at a minimum dose of 2 mg/kg (0.9 mg/lb) body weight once daily for up to 5 consecutive days (see WARNINGS and Animal Safety).

**For Prevention of Acute Vomiting in dogs 7 months of age and older:** Administer CERENIA Tablets orally at a minimum dose of 2 mg/kg (0.9 mg/lb) body weight once daily until resolution of acute vomiting.

If vomiting persists despite treatment, the case should be re-evaluated. CERENIA is most effective in preventing acute vomiting associated with chemotherapy if administered prior to the chemotherapeutic agent.

##### For Prevention of Vomiting Due to Motion Sickness in dogs 4 months and older

**For Prevention of Vomiting due to motion sickness in dogs 4 months of age and older:** Administer CERENIA Tablets orally at a minimum dose of 8 mg/kg (3.6 mg/lb) body weight once daily for up to 2 consecutive days (see WARNINGS and Animal Safety).

Administer CERENIA Tablets a minimum of two hours prior to travel with a small amount of food to mitigate vomiting associated with administration of the dose on an empty stomach; however, refrain from feeding a full meal prior to travel.

#### WARNINGS:

Not for use in humans. Keep out of the reach of children. In case of accidental ingestion, seek medical advice. Topical exposure may elicit localized allergic skin reactions in some individuals. Repeated or prolonged exposure may lead to skin sensitization. Wash hands with soap and water after administering drug. CERENIA is also an ocular irritant. In case of accidental eye exposure, flush with water for 15 minutes and seek medical attention.

In puppies younger than 11 weeks of age, histological evidence of bone marrow hypocellularity was observed at higher frequency and greater severity in puppies treated with CERENIA compared to control puppies. In puppies 16 weeks and older, bone marrow hypocellularity was not observed (see **ANIMAL SAFETY**).

#### PRECAUTIONS:

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

The safe use of CERENIA has not been evaluated in dogs with gastrointestinal obstruction, or dogs that have ingested toxins.

Use with caution in dogs with hepatic dysfunction because CERENIA is metabolized by CYP3A enzymes (see **Pharmacokinetics**). Use with caution with other medications that are highly protein bound. The concomitant use of CERENIA with other protein bound drugs has not been studied in dogs. Commonly used protein bound drugs include NSAIDs, cardiac, anticonvulsant, and behavioral medications. The influence of concomitant drugs that may inhibit the metabolism of CERENIA has not been evaluated. Drug compatibility should be monitored in patients requiring adjunctive therapy.

CERENIA causes dose related decreases in appetite and body weight (see **ANIMAL SAFETY**). To maximize therapeutic potential of CERENIA, the underlying cause of vomiting should be identified and addressed in dogs receiving CERENIA.

#### ADVERSE REACTIONS:

##### Prevention of Acute Vomiting (minimum of 2 mg/kg)

The following adverse reactions were reported during the course of a US field study for the prevention of acute vomiting in dogs treated with CERENIA Tablets at a minimum of 2 mg/kg orally and/or Injectable Solution at 1 mg/kg subcutaneously once daily for up to 5 consecutive days:

##### Frequency of Adverse Reactions by Treatment

Adverse Reaction	Placebo (n=69)		CERENIA (n=206)	
	# dogs	% occurrence	# dogs	% occurrence
Death during study	4	5.8	10	4.9
Euthanized during study	0	0	2	1
Diarrhea	6	8.7	8	3.9
Hematochezia/bloody stool	5	7.2	4	1.9
Anorexia	2	2.9	3	1.5
Otitis/Otorrhea	0	0	3	1.5
Endotoxic Shock	1	1.4	2	1
Hematuria	0	0	2	1
Excoriation	0	0	2	1

Other clinical signs were reported but were <0.5% of dogs.

##### Prevention of Vomiting Due to Motion Sickness (minimum of 8 mg/kg)

The following adverse reactions were reported during US studies for the prevention of vomiting due to motion sickness in dogs treated with CERENIA Tablets at a minimum of 8 mg/kg orally one time. Dogs may have experienced more than one of the observed adverse reactions.

##### Frequency of Adverse Reactions by Treatment

Adverse Reaction	Placebo (n=195)		CERENIA (n=208)	
	# dogs	% occurrence	# dogs	% occurrence
Hypersalivation	19	9.7	26	12.5
Vomiting <sup>1</sup>	0	0	11	5.3
Muscle Tremors	1	0.5	2	1
Sedation/Depression	3	1.5	2	1
Retching	3	1.5	1	0.5
Flatulence	0	0	1	0.5

<sup>1</sup> Not associated with motion sickness

The following adverse reactions were reported during a European field study for the prevention of vomiting due to motion sickness in dogs treated with CERENIA Tablets at a minimum of 8 mg/kg orally once daily for 2 consecutive days. Dogs may have experienced more than one of the observed adverse reactions.

##### Frequency of Adverse Reactions by Treatment

Adverse Reaction	Placebo (n=106)		CERENIA (n=107)	
	# dogs	% occurrence	# dogs	% occurrence
Vomiting	4	4	10	9
Drowsiness/Lethargy/Apathy	1	1	8	8
Hypersalivation	2	2	5	5
Anxiety	0	0	2	2
Trembling/Tremors	0	0	2	2
Inappetence	0	0	2	2
Mucus in stool	0	0	1	1

The following Adverse Reactions were reported during the conduct of a US clinical field trial where CERENIA Tablets were administered once daily for 28 consecutive days to 32 dogs: lethargy, vomiting, inappetence, corneal edema, and enlarged lymph nodes.

#### Post-Approval Experience

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

The following adverse events are listed in decreasing order of reporting frequency in dogs: depression/lethargy, anorexia, hypersalivation, vomiting, diarrhea, ataxia, and trembling.

Cases of ineffectiveness have been reported.

To report suspected adverse events, for technical assistance or to obtain a copy of the SDS, contact Zoetis Inc. at 1-888-963-8471 or [www.zoetis.com](http://www.zoetis.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>.

#### STORAGE CONDITIONS:

CERENIA Tablets should be stored at controlled room temperature 20°–25°C (68°–77°F) with excursions between 15°–30°C (59°–86°F).

#### HOW SUPPLIED:

CERENIA peach-colored tablets are scored with a break line, and contain 16, 24, 60 or 160 mg of maropitant as maropitant citrate per tablet. Each tablet is marked with "MPT" and the tablet strength on one side and the Pfizer logo on the other. Each tablet size is packaged in a bottle containing 60 tablets and packaged in blister packs containing 4 tablets per perforated sheet.

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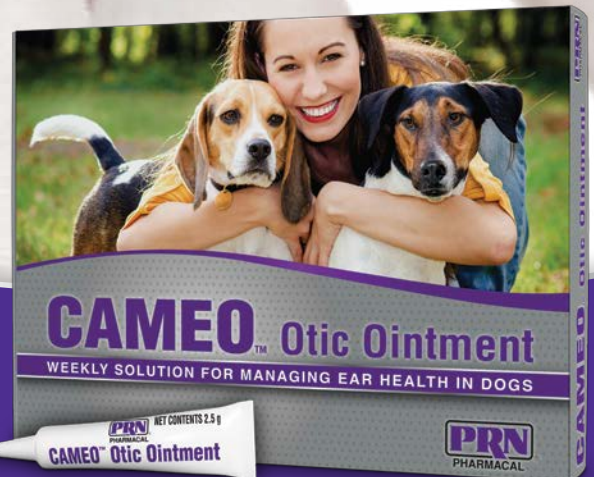
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# Cerebral Infarction

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## **P** Profile

### Definition

- *Cerebrovascular disease* refers to a group of disorders that result from a pathological process that compromises blood supply to the brain.
  - Such disorders may be either ischemic or hemorrhagic.
- Infarction is a local tissue injury or necrosis from reduced or absent blood flow to a specific part of the body, including the brain.
- Cerebral infarction (cerebral infarct, cerebrovascular accident [CVA], or stroke) is usually a *focal ischemic* event with an acute onset of asymmetric clinical signs that are progressive for a short time.
- *Global brain ischemia* can also occur (eg, anesthetic accidents, cardiopulmonary arrest).
- By definition, clinical signs must be present for at least 24 hours to be considered a stroke.<sup>1,2</sup>
- Transient ischemic attack (TIA) is the term used to describe a cerebrovascular disorder in which clinical signs resolve within 24 hours following transient ischemia.

### Pathophysiology

- There is little energy reserve in the brain, so it is dependent on continuous delivery of oxygen and glucose for energy; it is capable of only aerobic metabolism.<sup>1</sup>
- The brain receives 20% of cardiac output and accounts for 15% of oxygen consumption, despite comprising only 2% of body weight.<sup>1</sup>
- Infarcts can be described based on their underlying pathophysiology or location and size.

### Underlying Pathophysiology<sup>2,3</sup>

- *Ischemic infarct* is secondary to lack of oxygen delivery caused by blood vessel obstruction; this is the most common form of cerebral infarct in dogs and cats.
- *Hemorrhagic infarct* is secondary to ruptured blood vessels leading to hemorrhage within the brain parenchyma.

### Location & Size<sup>1,3</sup>

- *Territorial infarct* is a large area of tissue damage secondary to obstruction of one of the major arteries to the brain (eg, middle cerebral artery, rostral cerebellar artery).
- *Lacunar infarct* is a smaller area of tissue damage from obstruction of small superficial or deep penetrating arteries.



***Cerebrovascular disease* refers to a group of disorders that result from a pathological process that compromises blood supply to the brain.**

continues



**Predisposing Conditions for Cerebral Infarction**

- Aberrant parasite migration (eg, *Cuterebra* spp, *Dirofilaria immitis*)
- *Angiostrongylus vasorum* infection
- Atherosclerosis
- Cardiac disease
- Coagulopathy
- Chronic kidney disease
- Extension of CNS infection
- Hyperadrenocorticism
- Hyperlipidemia
- Hypertension
- Hypothyroidism
- Increased blood viscosity (eg, polycythemia, multiple myeloma)
- Intravascular neoplasia (eg, lymphoma, hemangiosarcoma)
- Liver disease
- Protein-losing nephropathy
- Sepsis and bacterial thromboembolism
- Vasculitis

**Table 1. Ancillary Diagnostics**

Ischemic infarction	Hemorrhagic infarction
Urine protein:creatinine ratio if proteinuria	Rickettsial disease testing
Endocrine testing for hyperadrenocorticism (eg, ACTH stimulation test, dexamethasone suppression testing)	Clotting studies: buccal mucosal bleeding time, prothrombin time (PT), activated partial thromboplastin time (APTT)
Serum antithrombin III activity	von Willebrand factor analysis
D-dimer tests	Testing for <i>Angiostrongylus vasorum</i> in endemic regions
Echocardiography and electrocardiography if underlying cardiac condition	

**Signalment**

- Infarction can occur at any age but is typically diagnosed in middle-aged to geriatric dogs and cats.<sup>4-6</sup>
- No apparent gender predisposition.
- They can occur in all breeds of dogs and cats, but the following breeds may be at increased risk<sup>6-10</sup>:
  - Greyhounds: Especially cerebellar infarcts; these are often idiopathic but may be hypertension-related.
  - Cavalier King Charles spaniels: Possibly related to local alterations in intracranial pressure secondary to Chiari-like malformation.
  - Miniature schnauzers: Possibly related to hyperlipidemia.
  - Brachycephalic breeds: Increased risk for global ischemia, especially with ketamine anesthetic protocols.

**Risk Factors**

- The three most common risk factors for cerebral infarction are hypertension, hypercoagulability, and hyperviscosity.

**Predisposing Conditions<sup>2,4,6,11</sup>**

- The most common predisposing causes are idiopathic hypertension, chronic kidney disease, and hyperadrenocorticism.

- A predisposing condition is identified in just over half of dogs with MRI evidence of infarction.
- See **Predisposing Conditions for Cerebral Infarction**.

**History**

- Patients are usually presented for evaluation following peracute to acute onset of neurologic signs that are non-progressive after 24 hours.
  - Rarely, progression may occur at 48-72 hours because of secondary cerebral edema.<sup>1,2</sup>
- Common clinical signs noted by owners include vestibular dysfunction, seizures, altered mental status, paresis, or ataxia.

**Physical Examination**

- General examination may be normal or demonstrate changes consistent with a predisposing condition (eg, cranial abdominal organomegaly, thin hair coat).
- Retinal fundic examination is recommended.
  - Hypertension may cause enlarged or tortuous retinal vessels.
  - Papilledema may be present if increased intracranial pressure.
  - Concurrent chorioretinitis or infil-

DWI = diffusion weighted images

trative disease (eg, lymphoma) further suggests presence of a concurrent, predisposing condition.

### Neurologic Examination

- As with all neurologic disorders, neurologic signs reflect lesion location and extent rather than cause.
- Common signs based on lesion location include:
  - Cerebrum: Seizures, mental obtundation, circling, pacing, inappropriate elimination
  - Thalamus: Signs of cerebral disease as above or vestibular dysfunction (possibly from damaged thalamic relay centers associated with cerebellar and vestibular nuclei; damage to the medial longitudinal fasciculus; input of vestibular information to the thalamus; or diaschisis, a sudden change in function in one area of the brain from damage in a distant location).
  - Brainstem: Altered mental status, cranial nerve deficits, vestibular dysfunction, paresis, ataxia.
  - Cerebellum: Paradoxical central vestibular dysfunction, hypermetria, cerebellar (intention) tremors, truncal sway/ataxia.

## **Dx** Diagnosis

### Definitive Diagnosis

- Definitive diagnosis requires histopathology at necropsy.
  - CT- or MRI-guided stereotactic biopsy may not provide a definitive diagnosis of infarction but may help rule out other possible causes (eg, neoplasia, encephalitis).
- A presumptive diagnosis can be made via advanced imaging and exclusion of other potential causes.

### Differential Diagnoses

- Intracranial neoplasia
- Immune-mediated, non-infectious encephalitis (eg, granulomatous meningoencephalomyelitis, necrotizing encephalitis)
- Infectious encephalitis
- Traumatic brain injury

### Laboratory Findings

- Minimum database includes CBC, serum chemistry panel, thyroid hormone analysis, and urinalysis.
- Serial systolic blood pressure measurements should be obtained to rule out systemic hypertension.
- Thoracic radiographs and abdominal ultrasound are recommended to screen for neoplasia and predisposing conditions.
- Ancillary diagnostics should be

performed based on the type of infarction present (**Table 1**, previous page).

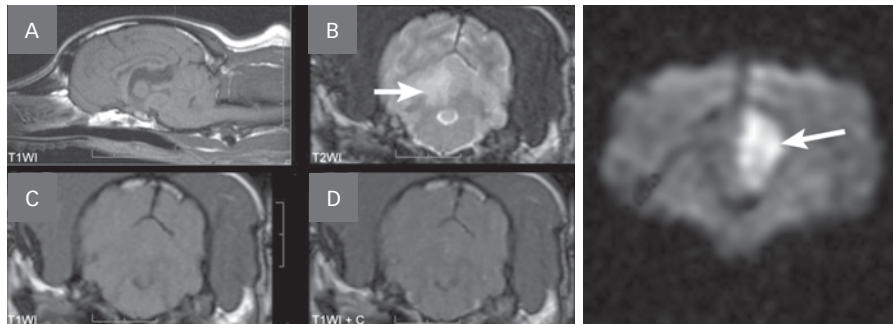
### Imaging

- MRI is the advanced imaging modality of choice given its superior soft tissue resolution.
  - The classic MRI characteristic of an ischemic stroke (**Figure 1**, next page) is an intra-axial lesion (often wedge-shaped) that is hyperintense (bright) on T2-weighted and fluid attenuation inversion recovery (FLAIR) images, iso- to hypointense (dark) on pre-contrast T1-weighted images, and minimal to no contrast enhancement.
  - Diffusion weighted imaging (DWI; **Figure 2**, next page) is the sequence of choice for acute ischemic infarction.
    - DWI detects lack of normal Brownian motion of molecules, particularly lack of intercellular water movement from cell swelling associated with cytotoxic edema.
    - An acute infarction appears as a hyperintense region.
  - The MRI appearance of hemorrhagic infarction (**Figure 3**, next page) varies greatly as blood cells and hemoglobin degrade (**Table 2**).

**Table 2. MRI Characteristics of Hemorrhage**

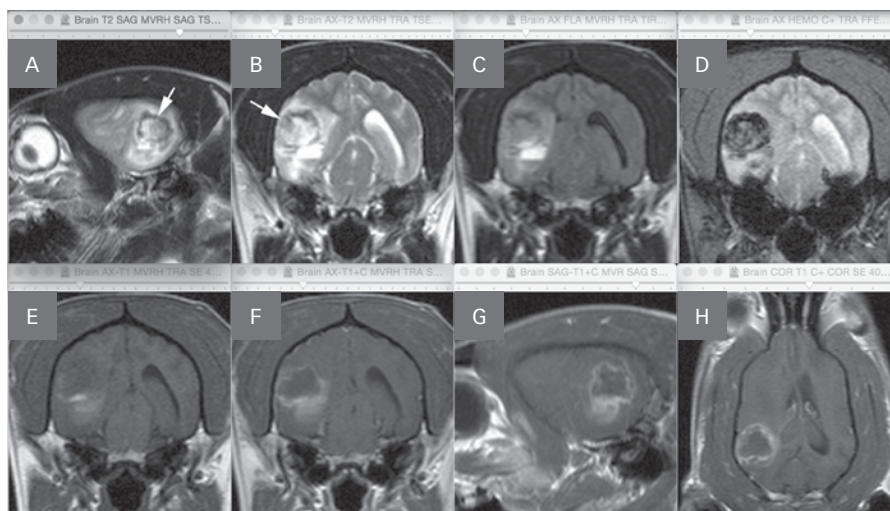
Stage	Time frame	Hemoglobin state	T2-weighted	T1-weighted
Peracute	<24 hrs	Oxyhemoglobin	Hyperintense	Isointense
Acute	1-3 days	Deoxyhemoglobin	Hypointense	Isointense
Early subacute	3-7 days	Intracellular methemoglobin	Hypointense	Hyperintense
Late subacute	>7 days	Extracellular methemoglobin	Hyperintense	Hyperintense
Chronic	>14 days	Hemosiderin	Hypointense	Iso- to hypointense

continues



**1** MRI images of a dog with a right cerebellar infarct (A). Note the wedge-shaped intra-axial lesion in the right dorsal cerebellar gray matter (arrow) that is hyperintense on T2-weighted images (B), isointense on T1-weighted images (C), and does not contrast enhance (D).

**2** DWI obtained from a dog showing a wedge-shaped, markedly hypointense signal in the left dorsal cerebellar gray matter consistent with a left cerebellar infarct (arrow). DWI is the MRI sequence of choice for peracute to acute infarction.



**3** MRI images from a dog with a presumed hemorrhagic infarct (arrows) based on improved clinical signs and reduction in size on follow-up MRI imaging without definitive treatment. There is a large, intra-axial lesion in the right parietal & occipital lobes. Images (A) and (G) are parasagittal T2-weighted and T1-weighted images, respectively. Images (B) through (F) are transverse images at the level of the left midbrain. Image (H) is a dorsal view. The lesion is heterogeneous and primarily hyperintense on T2-weighted (A, B) and FLAIR (C) images; hypointense on T2\*GRE (D) images consistent with hemorrhage; hypointense with a rim of hyperintensity on T1-weighted images (E); and has moderate-to-marked peripheral rim contrast enhancement (F-H).

- Hemorrhagic infarcts can be difficult to distinguish from hemorrhagic brain tumors (eg, glioma, hemangiosarcoma).
- The T2\*-gradient echo (T2\*GRE) sequence is best for identifying hemorrhage as it is hypointense on this sequence.
- T2\*GRE is also hypointense for mineralization, air, iron, melanin, and foreign bodies.

## Tx Treatment

### Inpatient or Outpatient

- Patients with mild signs may be treated on an outpatient basis.
- Non-ambulatory patients with moderate to severe clinical signs, especially larger-breed dogs, may need to be hospitalized until they are able to walk with minimal to no assistance.

### Acute Medical Treatment

- In general, there is no specific treatment for cerebral infarction.
- So-called *clot busters* or thrombolytic agents (eg, tissue plasminogen activator [tPA], streptokinase) are frequently used in human medicine.
  - These medications are infrequently used in veterinary medicine because blood clots are rarely a cause of infarction in dogs and cats, thrombolytic agents need to be given within 6 hours of infarction, and expense or limited availability preclude their use.
- Mannitol (0.5-1.0 g/kg IV over 10-15 minutes) or hypertonic saline 7.5% (3-5 mL/kg IV over 10-15 minutes) may be needed to reduce brain swelling.
  - There is a theoretical risk for exacerbating hemorrhage or cerebral edema if mannitol is given to patients with intracranial hemorrhage, but benefits likely outweigh risks.
- Hypertension should be treated to prevent ongoing damage.
  - Initial treatment recommendations include enalapril (dogs, 0.5 mg/kg PO q12h) or amlodipine (cats, 0.625-1.25 mg per cat PO daily).
- Oxygen support is recommended in moderate to severe cases, especially if hypoventilation is present.
- Nursing care for recumbent patients is critical and includes frequent turning and thick bedding to prevent pressure

sores, urinary catheterization if indicated, and physical rehabilitation (at a minimum, passive range of motion and massage).

### Chronic Medical Treatment

- Underlying predisposing conditions should be treated as indicated to reduce the risk for future infarction.
- Antithrombotics may be considered if a thromboembolic disorder is proven, but their use is controversial and not proven to be beneficial.
  - Options include clopidogrel (dogs, 1 mg/kg PO q24h; cats, 18.75 mg per cat PO q24h) or aspirin (dogs, 0.5-1.0 mg/kg/q24h; cats, 40 mg [1/2 baby aspirin tab] PO q48-72h

### Nutritional Aspects

- There are no specific nutritional recommendations for infarction, but diets higher in essential fatty acids and omega-3 may be helpful.<sup>12</sup>
- Diet recommendations should also be based on predisposing conditions, such as a low-protein diet in patients with kidney disease.

### Activity

- There are no activity restrictions for this condition.
- Physical rehabilitation is highly recommended to improve recovery and shorten duration of signs.

### Client Education

- Clients should be taught how to provide nursing care for recumbent animals, as well as how to treat underlying predisposing conditions.



### Follow-up

#### Patient Monitoring

- Patients should be monitored for signs of progression that might be consistent with a diagnosis other than stroke.

- If signs are progressive, further examination is required as that would suggest the patient *did not* have a stroke.
- Clients should be instructed to observe for signs of recumbency-associated aspiration pneumonia (eg, coughing, tachypnea, dyspnea).

### Complications

- The most common complication is recumbency-associated aspiration pneumonia.
- Other complications may be observed depending on concurrent predisposing conditions.



### In General

#### Relative Cost

- Diagnostic workup and acute treatment: \$\$\$\$-\$\$\$\$\$
- Chronic treatment and follow-up: \$\$-\$\$\$

#### Cost Key

\$ = up to \$100  
\$\$ = \$101-\$250  
\$\$\$ = \$251-\$500  
\$\$\$\$ = \$501-\$1000  
\$\$\$\$\$ = more than \$1000

### Prognosis

- In general, the prognosis for recovery is good to excellent for patients with focal infarctions that have limited initial clinical abnormalities, if given enough time and supportive care.
- Some patients have residual clinical signs, but quality of life is acceptable for most patients.
- The prognosis for global brain ischemia is guarded to fair. ■ **cb**

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# The Ehmer Sling in Canine Orthopedic Surgery

**James K. Roush, DVM, MS, DACVS**  
**Walter C. Renberg, DVM, MS, DACVS**  
*Kansas State University*

## Case Selection & Management

Proper case selection for Ehmer or Figure-8 sling use is critical to a successful outcome. The Ehmer sling was designed to maintain the head of the femur in the acetabulum after closed reduction of a craniodorsal coxofemoral luxation, to prevent weight bearing, and to limit hip motion during healing. It should not be used in dogs with ventral coxofemoral luxation, which should be treated with hobbles to prevent limb abduction.

Best results are obtained in dogs with acute luxations <24 hours in duration with temperaments amenable to confinement and continual bandage care. Ehmer slings should not be applied to dogs with luxations of >1 week duration, luxations associated with fractures of the adjacent acetabulum, poor hip conformation (hip dysplasia), or dogs that are unable to ambulate on the contralateral limb. Ehmer slings can be difficult to apply in obese or chondrodystrophic dogs. Ehmer slings may be useful after internal fixation of acetabular or femoral head and neck fractures to temporarily prevent weight bearing.

Success of Ehmer sling application is enhanced by appropriate technique during reduction. Hip radiographs must be taken and evaluated before reduction to identify dogs with acetabular fractures or ventral luxations and are not candidates for Ehmer sling application. Reduction should be attempted in anesthetized dogs with craniodorsal hip luxations. Reductions are best accomplished by a manipulative sequence composed of external rotation of the affected limb while simultaneously providing distal traction to the limb and countertraction to the inguinal area. While traction is maintained, the limb should be internally rotated and simultaneous distal pressure to the greater trochanter applied to facilitate reduction. After reduction and before sling application, the coxofemoral joint should be put through multiple complete range-of-motion exercises while medial pressure is applied to the greater trochanter to clear the acetabulum. Orthogonal radiographs of the affected hip should be performed and evaluated after Ehmer application to confirm reduction of the coxofemoral joint.

## Aftercare

Daily examination of the hip and Ehmer sling determines effectiveness of the sling for maintenance of internal rotation, flexion of the coxofemoral joint, and limb abduction. Loss of internal rotation, hip flexion, or abduction are indications for immediate sling replacement. The position of the greater trochanter in ventral relationship to a line that connects the ilial wing and ischiatic tuberosity should be palpated daily to confirm continued hip reduction, and the joint should be palpated through a shortened



## What You Will Need

- 1 to 2 rolls of 2-inch wide porous, nonelastic adhesive tape.

## Author Insight

**Best results are obtained in lean, calm dogs with acute luxations <24 hours in duration.**

continues

range of motion to confirm continued smooth function. The flank, abdomen, and distal limb are examined daily for sores, inflammation, and edema. If pressure sores or wounds develop, modify the sling or remove it immediately. Monitor the abdominal band in male dogs for urine contamination and irritation of the underlying skin.

Maintain the Ehmer sling for a minimum of 7 to 10 days (maximum, 14 days) and remove only after coxofemoral reduction is confirmed by repeated orthogonal radiographs. Relaxation rates of 15% to 71% have been reported after closed reduction<sup>1</sup>; however, the specific relaxation rate after closed reduction and Ehmer sling application has not been reported. Owner evaluation scores are better after closed reduction than after femoral head and neck excision, extracapsular suture stabilization, and

De Vita pinning.<sup>2</sup> Direct comparisons of recurrence rates or owner satisfaction between closed reduction, Ehmer sling, and more recently developed techniques (eg, toggle pin, rod repair) have not yet been reported.

Dogs should be kept under cage confinement for the period of Ehmer sling application and for a minimum of 4 weeks after removal. Voluntary use of the limb by the patient should begin within 1 or 2 days as stiffness decreases, then gradually increase on a daily basis following removal of the sling. Gentle physical rehabilitation consisting of daily hip range-of-motion exercises can be initiated 4 to 6 weeks after sling removal. Controlled leash walks or underwater treadmill therapy may also be beneficial to restore normal use and function.

### STEP-BY-STEP ■ EHMER SLING APPLICATION (AFTER CLOSED HIP REDUCTION)

#### STEP 1

Place the dog in lateral recumbency with the affected limb up. Flex the limb, and place it in slight internal rotation. Two to 3 layers of cast padding may be placed around the metatarsal area initially but can lead to increased incidence of bandage slippage.

#### STEP 2

Place the adhesive tape on the metatarsal area by placing it around the caudal surface with the adhesive side of the tape against the limb or initial wrap. Wrap the tape so the adhesive sides meet cranially and do not completely encircle the metatarsal. Take care not to place the tape tightly or completely around the metatarsus.



Images courtesy of Wiley-Blackwell. Reprinted from: Swaim SF, Renberg WC, Shike KM. *Small Animal Bandaging, Casting, and Splinting Techniques*. 1st ed. Ames, IA: Wiley-Blackwell; 2011:100-104.



### STEP 3

Bring the tape up the medial aspect of the crus and around the cranial aspect of the thigh proximal to the stifle with the adhesive side against the animal.



**Author Insight**  
**Preoperative hip radiographs *must* be taken and assessed to exclude dogs with acetabular fractures, femoral head fragments, and dogs with ventral luxations.**

### STEP 4

Continue to wrap tape around the caudal aspect of the crus and onto the medial side of the hock to finish caudally on the metatarsal area (A). When this portion of the bandage is completed, the lateral aspect of the j3 should be visible and internal rotation should be maintained. Steps 3 and 4 are repeated several times to strengthen and reinforce the bandage (B).

**Author Insight**  
**Perform daily examination of the hip and Ehmer sling to assess continued hip reduction and lack of bandage complications.**



continues

**STEP 5**

An abdominal support portion of the sling is necessary to maintain hip flexion and limb abduction and begins with the tape applied at the metatarsal region as described in Step 3.



**STEP 6**

Bring tape up the lateral aspect of the limb and then over the dorsum of the animal, cranial to the tuber coxae, with the adhesive side against the animal. To avoid shifts of loose skin that might let the limb extend as the animal stands, pull skin of the flank ventrally (**arrow**) before applying tape.



**STEP 7**

Continue to tape around the opposite side of the animal and abdomen. Place tape cranially to the prepuce on male dogs (A). Repeat Steps 5, 6, and 7 several times to strengthen and reinforce the sling. When the sling is complete, the limb should be abducted and flexed, with slight internal rotation (B). ■ **cb**



**Author Insight**

**Before application of the splint, mild external rotation of the hip should be performed to assess the degree of stability. Dogs with excessive laxity or easy luxation are not candidates for Ehmer sling application.**



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\*R.C. Gupta et al., J Anim Physiol Anim Nutrition, 96:770-777,2012.  
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# Regenerative Therapy for Canine Myocardial Disease

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Regenerative medicine involves the use of stem cell and gene-replacement therapy—either as single modalities or in combination—to manipulate the body's capacity for repair. Stem cells are undifferentiated, self-renewing cells that possess a multi-lineage differentiation potential with the capacity to regenerate, repair, or substitute damaged tissue, allowing the re-establishment of its function.

The mechanism of action of stem cells involves several pathways<sup>1</sup> and is largely dependent on the type of cell (eg, skeletal myoblasts, bone-marrow–derived cells, embryonic stem cells, endogenous cardiac stem cells, and induced pluripotent stem cells) (Figure 1).

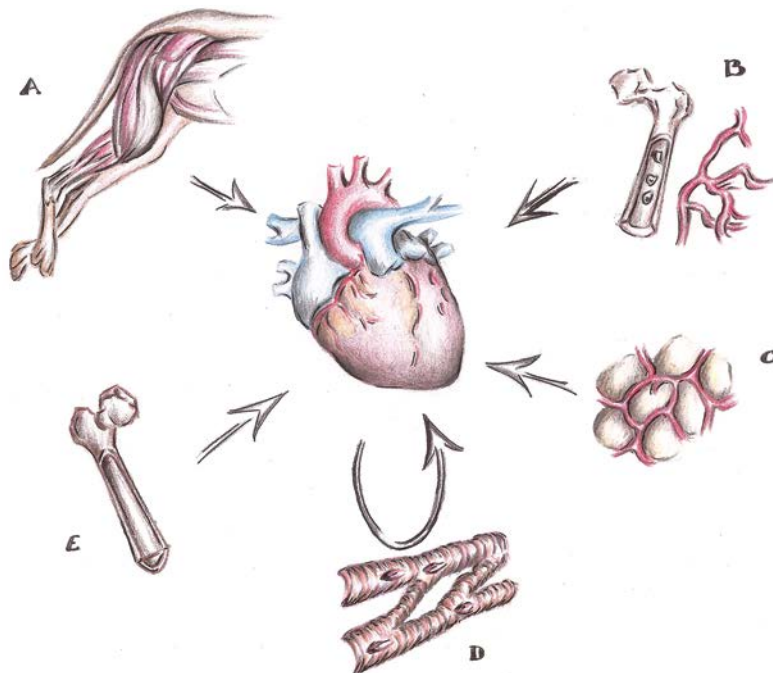
For example, pluripotent stem cells are capable of differentiating into all cell types, including cardiomyocytes, but multipotent and unipotent stem cells can only differentiate into a limited number of cell types. Cardiac stem cells are capable of differentiating into myocytes, endothelial cells, and vascular smooth muscle cells.

Gene-replacement therapy has the potential to become an ideal treatment for inherited diseases for which the mutant gene has been identified. It has traditionally been used to transfer a gene that encodes a functional protein into a diseased patient to produce long-term expression of the deficient protein<sup>2,3</sup> using a viral vector (eg, adeno-associated virus [AAV]); this can regenerate lost tissue (Figure 2, next page).

## Indications and Advantages

In cardiovascular medicine, most cardiac stem cell therapies have been directed toward myocardial repair following acute and chronic myocardial infarction in humans. Studies in cardiac stem cell therapy have shown that transplantation of mesenchymal stem cells improves cardiac function in rats, rabbits, and humans with dilated cardiomyopathy.<sup>4-9</sup>

Dilated cardiomyopathy (DCM) is the most common adult-onset acquired myocardial disease that affects large- and giant-breed dogs. Doberman pinschers are affected by the most common and severe form of DCM in veterinary medicine.<sup>10</sup> The disease can progress to cause refractory congestive heart failure or sudden death.



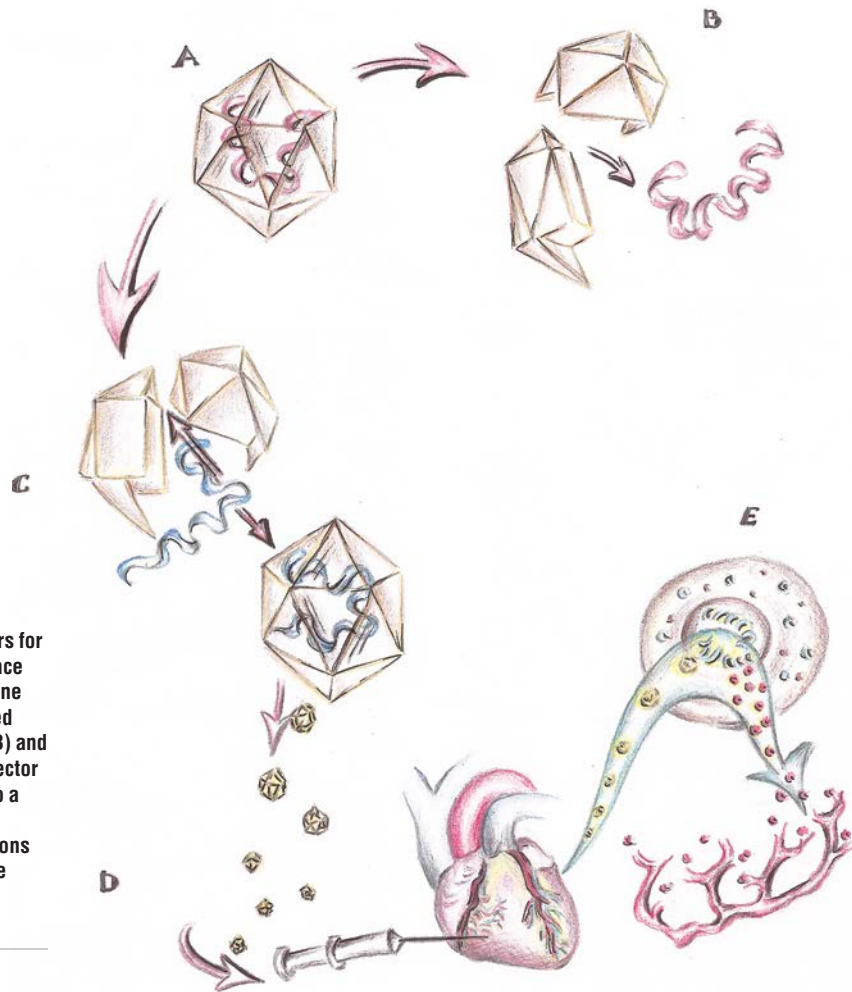
1

**Types of stem cells used for cardiac regenerative therapy to restore heart function directly. Multipotent and unipotent stem cells originating from skeletal myoblasts (A), bone marrow and blood endothelial progenitor cells (B), adipose-derived cells (C), resident cardiac stem cells (D), and bone marrow (E).**

Images courtesy of Paola Longo, MD, head of the vascular diagnostic operative unit at San Filippo Neri Hospital, Rome, Italy.

**Gene-replacement therapy has the potential to become an ideal treatment for inherited diseases for which the mutant gene has been identified.**

**How many cells it takes to regenerate the entire myocardium and how many cells can safely be used remains to be seen.**



**2** Therapeutic gene transfer using viral vectors for gene delivery reengineers the virus to replace the viral disease-causing genes with the gene of interest (ie, the therapeutic gene). In this simplified schematic, an AAV (A) has its viral genes removed (B) and a therapeutic gene of interest added (C). This viral vector package containing therapeutic genes is injected into a patient (D). The vector virus binds to host cells and introduces therapeutic genetic material (and directions for producing more copies of the virus) as part of the replication process (E).

Conventional palliative medical therapy with diuretics, ACE-inhibitors, inodilators, and anti-arrhythmic drugs has assisted in management of these cases but does not correct underlying cardiac muscle cell dysfunction. Advanced therapeutic strategies used in human medicine, such as cardiac transplantation, implantation of mechanical-assist devices, and cardiac resynchronization therapy, are invasive and generally cost prohibitive for veterinary patients.

A specific genetic mutation (pyruvate dehydrogenase kinase gene [*PDK4*]) has been identified in Doberman pinschers with DCM.<sup>11</sup> This offers a potential new avenue for research aimed at identifying better treatment options for this disease.

Regenerative therapy with gene-replacement therapy alone or in combination with stem cells has been used with various levels of success to treat diseases where a specific genetic mutation has been identified (eg, canine hemophilia, lysosomal storage diseases, inherited retinal diseases<sup>12-18</sup>). This may also be a viable treatment option for Doberman pinschers with DCM and the

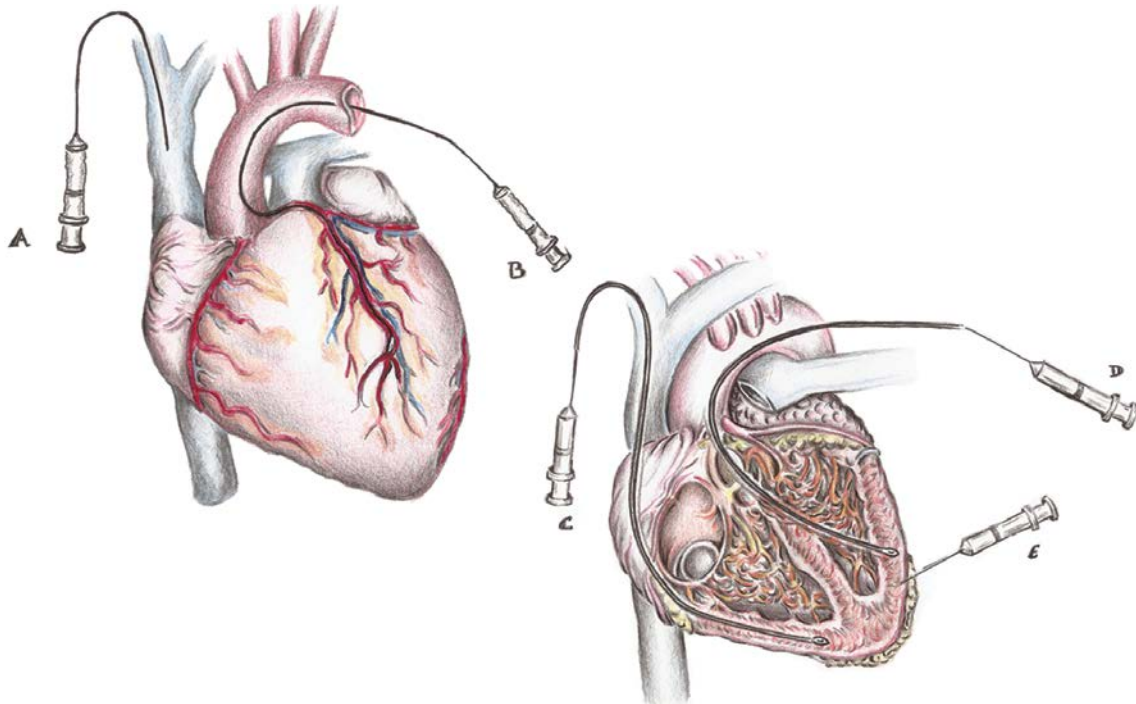
recently identified *PDK4* mutation as well as other cardiac diseases in veterinary medicine for which a genetic mutation has been identified.

### Challenges and Disadvantages

Challenges of global cardiac regeneration using stem cells and gene therapy involve 4 areas:

- Identification of ideal cell types and vectors
- Identification of the dose required for global cardiac regeneration
- Identification of the best route of cell and/or vector delivery
- Development of a safe and effective product.

A rational approach to the study of cardiac disease is needed to understand the mechanisms that may improve myocardial performance. A wide variety of cell types (eg, skeletal myoblasts, bone-marrow-derived cells, embryonic stem cells, endogenous cardiac stem cells) and vectors (eg, AAV2, AAV6, AAV8, AAV9) have been considered as candidates for therapeutic delivery. It is



**3** Retention of cells immediately after delivery is highly dependent on the delivery strategy. Cells can be injected through several methods. Intravenously (A) is simplest and least invasive, but dilution of cells and/or vector by systemic blood circulation and cells and/or vectors uptake by other organs can pose potential challenges. Coronary artery infusion (B), in which the cells and/or vector are injected through the lumen of an inflated angioplasty catheter into the coronary artery and reside in the coronary circulation until balloon is deflated. Retrograde coronary venous sinus infusion (C), in which the cells and/or vector are

injected into the coronary sinus through the lumen of an inflated angioplasty catheter under pressure to disrupt endothelial borders and allow cells and/or vector to traverse into the myocardium. Direct intramyocardial involves injection of the cells and/or vector either endocardially (D) or epicardially (E). The primary advantage of this method is that cells and/or vectors delivery bypasses the endothelial barrier, which results in high local concentrations at the injection site.

still unknown which vector, type of stem cell or progenitor cell, or some combination of the 2 is the best option for achieving cardiac regeneration.

Cell numbers required to regenerate the entire myocardium and how many cells can be safely used is still unclear with regard to cell therapy in the treatment of global cardiac dysfunction.

Cardiomyocyte transduction (ie, the introduction of DNA into the cell via a viral vector) has proven more difficult in global cardiac dysfunction because myocardial volume is a determinant of the proportion of the myocardial mass that is transduced by the administration of a cell and/or vector. The percentage of the myocardium required to be successfully transduced for effective therapy is still unclear, and the required number of transduced cells may vary depending on the underlying cause of cardiomyopathy.<sup>19</sup>

Finding the appropriate dose is not the only determinant of good outcome. Another challenge for cardiac regeneration is determining the optimal route of delivery. Retention of cells immediately after delivery is highly dependent on the delivery strategy. Cells can be injected intravenously, into coronary arteries, or directly into the myocardium (Figure 3).

The IV route is safest and easiest, but studies have shown minimal dwell time, non-specific cardiac muscle targeting, and poor results. A large number of cells and/or vectors is required to achieve cardiac transduction to counter first-pass effect; this exponentially increases the cost of the treatment. There is also a concern regarding the intracoronary delivery route; administration in this manner may result in blockage of the coronary arteries and cause further damage to the myocardium.<sup>20,21</sup>

The development of an effective and safe product (a combination of a vector and stem cell or gene) is of utmost importance.

continues

AAV = adeno-associated virus, ACE = angiotensin-converting enzyme, DCM = dilated cardiomyopathy, *PK4* = pyruvate dehydrogenase kinase gene

The increased popularity of AAV vectors has prompted the FDA to regulate procedures, practices, and facilities for the implementation of methods that avoid genetic exchange between animals and humans.

## Clinical Impact

Regenerative therapy for cardiac disease is a growing area of research that has recently led to several clinical trials in humans. Strategies such as cell transplantation and reprogramming have demonstrated intriguing and exciting results.

When a specific genetic mutation is discovered, the use of a combined approach of stem cell and gene-replacement therapy to achieve cardiac regeneration is a real possibility that could change the progression of the disease.

## Future Directions

Not long ago, the heart was still considered a static and postmitotic organ that lacked regenerative capacity; it was thought that the number of cardiomyocytes in an individual was established at birth, and cardiomyocyte hypertrophy was considered the only cellular adaptive response of the heart.<sup>22</sup>

After more than a decade of research, views have changed comprehensively regarding cardiac remodeling and cardiac regenerative therapy as an important area of research. Several experimental studies were initiated with different types of stem cells. Because of the encouraging results, a rapid transition from preclinical experiments to clinical trials occurred.<sup>23</sup> Although clinical trials demonstrated that cardiac regenerative therapy is safe, it remains unclear why preclinical expectations were not met in the majority of the studies.<sup>23</sup>

The results of clinical trials and experiments demonstrate that much remains to be investigated before clinical applicability can become a reality. ■ **cb**

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# Reduced Fertility & Epididymitis in a Dog

**Cheryl Lopate, MS, DVM, DACT**

*Reproductive Revolutions & Wilsonville Veterinary Clinic  
Wilsonville, Oregon*

**A 4.5-year-old intact male Parson Russell terrier was presented for an infertility evaluation. He had been bred to multiple bitches over the last 2.5 years.**

## History

In the first year of his breeding career, he had excellent fertility, with all bitches being bred naturally and conceiving with normal-sized litters of 4 to 8 puppies each. At the start of the second year of his breeding career, his fertility was normal. However, in the previous 6 months, he had been bred to 4 bitches (2 from his own kennel, 2 from outside kennels), none of which whelped any puppies. One aborted her litter on day 52 of pregnancy.

## Examination

Physical examination revealed a temperature of 100.4° F, pulse at 120 bpm, respiration at 16 breaths/min, pink mucous membranes, and capillary refill time <2 seconds. There was mild retropharyngeal and submandibular lymphadenopathy. Auscultation of the heart and lungs was normal. Abdominal palpation was unremarkable. There was prominent scrotal dermatitis, and mild-to-moderate unilateral epididymal enlargement of the right epididymal head, body, and tail with concurrent thickening of the distal spermatic cord (**Figure 1**, next page). Both testes were slightly softer than expected but of normal size.



**Table 1. Semen Evaluation**

<b>Volume</b>	3 mL fractions 1 & 2 combined
<b>Total motility</b>	40%
<b>Progressive motility</b>	25%, velocity 3/5; mild head-head agglutination
<b>Total sperm/ejaculate</b>	453 million
<b>Morphology</b>	12% normal; 16% knobbed or detached acrosomes; 23% thickened midpieces; 14% proximal protoplasmic droplets; 8% distal midpiece reflexes; 14% bent tails; 13% detached heads
<b>Cytology of pellet sediment</b>	A moderate number of round cells noted on wet mount evaluation and a WBC count via hemocytometer revealed a WBC count of 22,000/μL. Stained cytology (Wright's stain) revealed a round cell population comprised of both neutrophils and macrophages.

WBC = white blood cell

## Ask Yourself



1. What are the differentials for epididymitis in this dog?
2. What methods of bacterial isolation are available for diagnosis of brucellosis?
3. What additional diagnostics can be used to identify brucellosis infection?
4. What modalities are available to treat *B canis* infection?
5. What concerns are there about interspecies or zoonotic transmission?

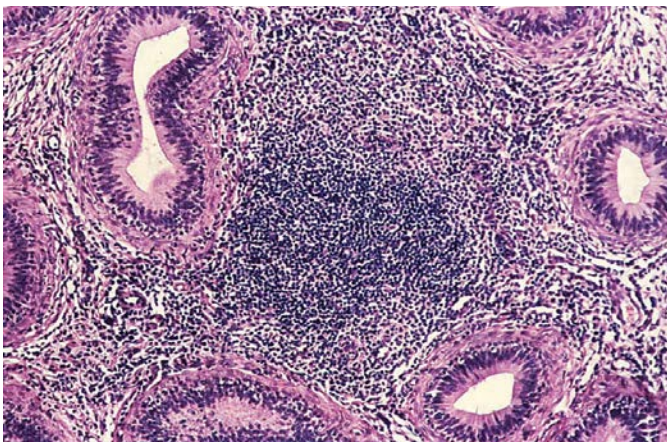
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### Diagnostic Results

Results of the semen evaluation, collected via manual stimulation, are provided in **Table 1** (previous page). There was no apparent pain associated with ejaculation.



**1** Chronic epididymitis with the head, body, and tail of the epididymis as well as the distal spermatic cord (enlarged and irregular) postcastration; the testicle is smaller and flatter than normal because of chronic infection.



**2** Prominent, diffuse lymphocytic inflammation commonly associated with *B canis* epididymitis.  
Images courtesy of Cornell Pathology Laboratory

### Further Diagnostic Testing

Enzyme-linked immunosorbent assay (ELISA) revealed a positive brucellosis status (*Brucella canis* infection), which was confirmed with agar gel immunodiffusion (AGID) testing. Qualitative semen culture was performed, and numerous *B canis* organisms were isolated along with moderate numbers of beta-hemolytic streptococci. The presence of white blood cells in semen cytology suggested a diagnosis of epididymitis. Histopathology demonstrates diffuse lymphocytic inflammation (**Figure 2**).

### Diagnosis

Canine brucellosis

### Treatment & Outcome

The state veterinarian was notified because brucellosis is a reportable disease in most states. The dog was castrated and quarantined for 8 months and was treated with tetracycline and streptomycin for 8 weeks. Serologic testing was performed on the remaining animals in the kennel. Seventy-five percent of the animals in the original kennel (21/28) were positive for *B canis*. In the kennels in which outside bitches had been bred, 100% of the animals in 1 kennel and 50% in another (3 and 4 animals, respectively) were infected. All positive animals were neutered and treated with tetracycline (22-50 mg/kg) or were euthanized if the owner did not want to quarantine and treat.

### Prevention

Serologic testing should be performed on all new arrivals to a breeding kennel, followed by 8 weeks of quarantine and retesting. Animals that are negative at this stage are considered safe to enter the general population and for breeding. Because brucellosis is a zoonotic disease, the importance of testing all new arrivals and other animals that are on the premises or that may have been exposed directly or indirectly cannot be overstated.

**Table 2. Commonly Used Serologic & Diagnostic Tests for Brucellosis**

Test	Antigen	Sensitivity & Specificity	Positive Predictive Value	Negative Predictive Value
RSAT + 2ME-RSAT	Cell wall	Very sensitive, low specificity	Low	High
TAT	Cell wall	High sensitivity, low specificity	Low	High
AGID	Cell wall	High sensitivity, good specificity	Moderate	High
PCR	DNA	Very sensitive, very specific	High	High

AGID = agar gel immunodiffusion, ELISA = enzyme-linked immunosorbent assay, PCR = polymerase chain reaction, TAT = tube agglutination test



## Did You Answer?

1. Differentials for epididymitis include aerobic bacterial or fungal infection; *Brucella canis* infection; infection via hematogenous or descending routes; sperm granuloma; trauma; or varicocele.
2. The ideal bacterial diagnostic isolation method for brucellosis is blood culture. Bacteremia occurs between 2 and 4 weeks post infection and lasts for approximately 6 months, becoming more intermittently isolated as 1 year post infection is reached. In some individuals, bacteria may be isolated for up to 5 years. Bacteria may also be isolated from semen, prostatic fluid, or urine. Following castration, the organism can be isolated from the testes; at the time of necropsy, the organism can be isolated from lymph nodes, spleen, liver, prostate, or bone marrow. Culture should only be performed in specialized laboratories because *Brucella* spp culture is associated with increased laboratory safety risks. Culture should never be performed in veterinary clinics if *Brucella* spp are potentially present.
3. Additional serologic testing can be performed using a variety of screening tests, including rapid slide macro- and microagglutination tests, tube agglutination test (TAT), ELISA, indirect immunofluorescence tests, complement fixation, counter-immunoelectrophoresis, or polymerase chain reaction (PCR) test (**Table 2**). AGID is considered the gold standard of testing and should be carried out when any of the other diagnostic tests are positive. Seroconversion will take a minimum of 6–8 weeks post infection, so any animal with a negative screening test but suspicious clinical signs should be isolated and retested in 2 months for confirmation.
4. Treatment is difficult because *B canis* is an intracellular organism; therefore, it can be difficult to achieve adequate concentrations of antibiotics to kill the organism. No antibiotic, alone or in combination, is 100% effective at eradication of the bacterium. Antibiotics that have been most effective include tetracycline or minocycline in combination with streptomycin or enrofloxacin. Gonadectomy is a requisite part of treatment. One should consider all animals that have been positive at any time as potentially infective later. Removal and strict isolation or euthanasia are ideal solutions and highly recommended for kennels.
5. Transmission may occur via aerosol contact with infected secretions or contaminated urine. Disinfection with

quaternary ammonium compounds and iodides will treat the environment; the organism does not live long outside the host unless organic material is present. The organism spreads rapidly in a kennel situation because of close contact between animals. Zoonotic transmission to humans is possible, resulting in presentations such as indolent fever and lymphadenopathy, pharyngitis, joint pain, and weight loss. ■ **cb**

### Suggested Reading

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**CHEWABLE TABLETS**

**Brief Summary:** Before using PREVICOX, please consult the product insert, a summary of which follows:

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

**Indications:** PREVICOX (firocoxib) Chewable Tablets are indicated for the control of pain and inflammation associated with osteoarthritis and for the control of postoperative pain and inflammation associated with soft-tissue and orthopedic surgery in dogs.

**Contraindications:** Dogs with known hypersensitivity to firocoxib should not receive PREVICOX.

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

**For oral use in dogs only. Use of this product at doses above the recommended 2.27 mg/lb (5.0 mg/kg) in puppies less than seven months of age has been associated with serious adverse reactions, including death (see Animal Safety). Due to tablet sizes and scoring, dogs weighing less than 12.5 lb (5.7 kg) cannot be accurately dosed.**

All dogs should undergo a thorough history and physical examination before the initiation of NSAID therapy. Appropriate laboratory testing to establish hematological and serum baseline data is recommended prior to and periodically during administration of any NSAID. **Owners should be advised to observe for signs of potential drug toxicity (see Adverse Reactions and Animal Safety) and be given a Client Information Sheet about PREVICOX Chewable Tablets.**

For technical assistance or to report suspected adverse events, call 1-877-217-3543.

**Precautions:** This product cannot be accurately dosed in dogs less than 12.5 pounds in body weight. Consider appropriate washout times when switching from one NSAID to another or when switching from corticosteroid use to NSAID use.

As a class, cyclooxygenase inhibitory NSAIDs may be associated with renal, gastrointestinal and hepatic toxicity. Sensitivity to drug-associated adverse events varies with the individual patient. Dogs that have experienced adverse reactions from one NSAID may experience adverse reactions from another NSAID. Patients at greatest risk for adverse events are those that are dehydrated, on concomitant diuretic therapy, or those with existing renal, cardiovascular, and/or hepatic dysfunction. Concurrent administration of potentially nephrotoxic drugs should be carefully approached and monitored. NSAIDs may inhibit the prostaglandins that maintain normal homeostatic function. Such anti-prostaglandin effects may result in clinically significant disease in patients with underlying or pre-existing disease that has not been previously diagnosed. Since NSAIDs possess the potential to produce gastrointestinal ulceration and/or gastrointestinal perforation, concomitant use of PREVICOX Chewable Tablets with other anti-inflammatory drugs, such as NSAIDs or corticosteroids, should be avoided. The concomitant use of protein-bound drugs with PREVICOX Chewable Tablets has not been studied in dogs. Commonly used protein-bound drugs include cardiac, anticonvulsant, and behavioral medications. The influence of concomitant drugs that may inhibit the metabolism of PREVICOX Chewable Tablets has not been evaluated. Drug compatibility should be monitored in patients requiring adjunctive therapy. If additional pain medication is needed after the daily dose of PREVICOX, a non-NSAID class of analgesic may be necessary. Appropriate monitoring procedures should be employed during all surgical procedures. Anesthetic drugs may affect renal perfusion, approach concomitant use of anesthetics and NSAIDs cautiously. The use of parenteral fluids during surgery should be considered to decrease potential renal complications when using NSAIDs perioperatively. The safe use of PREVICOX Chewable Tablets in pregnant, lactating or breeding dogs has not been evaluated.

**Adverse Reactions:**

**Osteoarthritis:** In controlled field studies, 128 dogs (ages 11 months to 15 years) were evaluated for safety when given PREVICOX Chewable Tablets at a dose of 2.27mg/lb (5.0 mg/kg) orally once daily for 30 days. The following adverse reactions were observed. Dogs may have experienced more than one of the observed adverse reactions during the study.

**Adverse Reactions Seen in U. S. Field Studies**

Adverse Reactions	PREVICOX (n=128)	Active Control (n=121)
Vomiting	5	8
Diarrhea	1	10
Decreased Appetite or Anorexia	3	3
Lethargy	1	3
Pain	2	1
Somnolence	1	1
Hyperactivity	1	0

PREVICOX (firocoxib) Chewable Tablets were safely used during field studies concomitantly with other therapies, including vaccines, anthelmintics, and antibiotics.

**Soft-tissue Surgery:** In controlled field studies evaluating soft-tissue postoperative pain and inflammation, 258 dogs (ages 10.5 weeks to 16 years) were evaluated for safety when given PREVICOX Chewable Tablets at a dose of 2.27 mg/lb (5.0 mg/kg) orally approximately 2 hours prior to surgery and once daily thereafter for up to two days. The following adverse reactions were observed. Dogs may have experienced more than one of the observed reactions during the study.

**Adverse Reactions Seen in the Soft-tissue Surgery Postoperative Pain Field Studies**

Adverse Reactions	Firocoxib Group (n=127)	Control Group* (n=131)
Vomiting	5	6
Diarrhea	1	1
Bruising at Surgery Site	1	1
Respiratory Arrest	1	0
SQ Crepitus in Rear Leg and Flank	1	0
Swollen Paw	1	0

\*Sham-dosed (pilled)

**Orthopedic Surgery:** In a controlled field study evaluating orthopedic postoperative pain and inflammation, 226 dogs of various breeds, ranging in age from 1 to 11.9 years in the PREVICOX-treated groups and 0.7 to 17 years in the control group were evaluated for safety. Of the 226 dogs, 118 were given PREVICOX Chewable Tablets at a dose of 2.27 mg/lb (5.0 mg/kg) orally approximately 2 hours prior to surgery and once daily thereafter for a total of three days. The following adverse reactions were observed. Dogs may have experienced more than one of the observed reactions during the study.

**Adverse Reactions Seen in the Orthopedic Surgery Postoperative Pain Field Study**

Adverse Reactions	Firocoxib Group (n=118)	Control Group* (n=108)
Vomiting	1	0
Diarrhea	2**	1
Bruising at Surgery Site	2	3
Inappetence/ Decreased Appetite	1	2
Pyrexia	0	1
Incision Swelling, Redness	9	5
Oozing Incision	2	0

A case may be represented in more than one category.

\*Sham-dosed (pilled).

\*\*One dog had hemorrhagic gastroenteritis.

**Post-Approval Experience (Rev. 2009):** The following adverse reactions are based on post-approval adverse drug event reporting. The categories are listed in decreasing order of frequency by body system:

**Gastrointestinal:** Vomiting, anorexia, diarrhea, melena, gastrointestinal perforation, hematemesis, hematochezia, weight loss, gastrointestinal ulceration, peritonitis, abdominal pain, hypersalivation, nausea

**Urinary:** Elevated BUN, elevated creatinine, polydipsia, polyuria, hematuria, urinary incontinence, proteinuria, kidney failure, azotemia, urinary tract infection

**Neurological/Behavioral/Special Sense:** Depression/lethargy, ataxia, seizures, nervousness, confusion, weakness, hyperactivity, tremor, paresis, head tilt, nystagmus, mydriasis, aggression, uveitis

**Hepatic:** Elevated ALP, elevated ALT, elevated bilirubin, decreased albumin, elevated AST, icterus, decreased or increased total protein and globulin, pancreatitis, ascites, liver failure, decreased BUN

**Hematological:** Anemia, neutrophilia, thrombocytopenia, neutropenia

**Cardiovascular/Respiratory:** Tachypnea, dyspnea, tachycardia

**Dermatological/Immunologic:** Pruritis, fever, alopecia, moist dermatitis, autoimmune hemolytic anemia, facial/muzzle edema, urticaria

In some situations, death has been reported as an outcome of the adverse events listed above.

For a complete listing of adverse reactions for firocoxib reported to the CVM see:

<http://www.fda.gov/AnimalVeterinary/SafetyHealth/ProductSafetyInformation/ucm055394.htm>

**Information For Dog Owners:** PREVICOX, like other drugs of its class, is not free from adverse reactions. 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, dark or tarry stools, increased water consumption, increased urination, pale gums due to anemia, yellowing of gums, skin or white of the eye due to jaundice, lethargy, incoordination, seizure, or behavioral changes. **Serious adverse reactions associated with this drug class can occur without warning and in rare situations result in death (see Adverse Reactions).** Owners should be advised to discontinue PREVICOX therapy and contact their veterinarian immediately if signs of intolerance are observed. The vast majority of patients with drug-related adverse reactions have recovered when the signs are recognized, the drug is withdrawn, and veterinary care, if appropriate, is initiated. Owners should be advised of the importance of periodic follow up for all dogs during administration of any NSAID.

**Effectiveness:** Two hundred and forty-nine dogs of various breeds, ranging in age from 11 months to 20 years, and weighing 13 to 175 lbs, were randomly administered PREVICOX or an active control drug in two field studies. Dogs were assessed for lameness, pain on manipulation, range of motion, joint swelling, and overall improvement in a non-inferiority evaluation of PREVICOX compared with the active control. At the study's end, 87% of the owners rated PREVICOX-treated dogs as improved. Eighty-eight percent of dogs treated with PREVICOX were also judged improved by the veterinarians. Dogs treated with PREVICOX showed a level of improvement in veterinarian-assessed lameness, pain on palpation, range of motion, and owner-assessed improvement that was comparable to the active control. The level of improvement in PREVICOX-treated dogs in limb weight bearing on the force plate gait analysis assessment was comparable to the active control. In a separate field study, two hundred fifty-eight client-owned dogs of various breeds, ranging in age from 10.5 weeks to 16 years and weighing from 7 to 168 lbs, were randomly administered PREVICOX or a control (sham-dosed-pilled) for the control of postoperative pain and inflammation associated with soft-tissue surgical procedures such as abdominal surgery (e.g., ovariohysterectomy, abdominal cryptorchidectomy, splenectomy, cystotomy) or major external surgeries (e.g., mastectomy, skin tumor removal <8 cm). The study demonstrated that PREVICOX-treated dogs had significantly lower need for rescue medication than the control (sham-dosed-pilled) in controlling postoperative pain and inflammation associated with soft-surgery. A multi-center field study with 226 client-owned dogs of various breeds, and ranging in age from 1 to 11.9 years in the PREVICOX-treated groups and 0.7 to 17 years in the control group was conducted. Dogs were randomly assigned to either the PREVICOX or the control (sham-dosed-pilled) group for the control of postoperative pain and inflammation associated with orthopedic surgery. Surgery to repair a ruptured cruciate ligament included the following stabilization procedures: fabellar suture and/or imbrication, fibular head transposition, tibial plateau leveling osteotomy (TPO), and 'over the top' technique. The study (n = 220 for effectiveness) demonstrated that PREVICOX-treated dogs had significantly lower need for rescue medication than the control (sham-dosed-pilled) in controlling postoperative pain and inflammation associated with orthopedic surgery.

**Animal Safety:** In a targeted animal safety study, firocoxib was administered orally to healthy adult Beagle dogs (eight dogs per group) at 5, 15, and 25 mg/kg (1, 3, and 5 times the recommended total daily dose) for 180 days. At the indicated dose of 5 mg/kg, there were no treatment-related adverse events. Decreased appetite, vomiting, and diarrhea were seen in dogs in all dose groups, including unmedicated controls, although vomiting and diarrhea were seen more often in dogs in the 5X dose group. One dog in the 3X dose group was diagnosed with juvenile polyarteritis of unknown etiology after exhibiting recurrent episodes of vomiting and diarrhea, lethargy, pain, anorexia, ataxia, proprioceptive deficits, decreased albumin levels, decreased and then elevated platelet counts, increased bleeding times, and elevated liver enzymes. On histopathologic examination, a mild ileal ulcer was found in one 5X dog. This dog also had a decreased serum albumin which returned to normal by study completion. One control and three 5X dogs had focal areas of inflammation in the pylorus or small intestine. Vacuolization without inflammatory cell infiltrates was noted in the thalamic region of the brain in three control, one 3X, and three 5X dogs. Mean ALP was within the normal range for all groups but was greater in the 3X and 5X dose groups than in the control group. Transient decreases in serum albumin were seen in multiple animals in the 3X and 5X dose groups, and in one control animal. In a separate safety study, firocoxib was administered orally to healthy juvenile (10-13 weeks of age) Beagle dogs at 5, 15, and 25 mg/kg (1, 3, and 5 times the recommended total daily dose) for 180 days. At the indicated (1X) dose of 5 mg/kg, on histopathologic examination, three out of six dogs had minimal periportal hepatic fatty change. On histopathologic examination, one control, one 1X, and two 5X dogs had diffuse slight hepatic fatty change. These animals showed no clinical signs and had no liver enzyme elevations. In the 3X dose group, one dog was euthanized because of poor clinical condition (Day 63). This dog also had a mildly decreased serum albumin. At study completion, out of five surviving and clinically normal 3X dogs, three had minimal periportal hepatic fatty change. Of twelve dogs in the 5X dose group, one died (Day 82) and three moribund dogs were euthanized (Days 38, 78, and 79) because of anorexia, poor weight gain, depression, and in one dog, vomiting. One of the euthanized dogs had ingested a rope toy. Two of these 5X dogs had mildly elevated liver enzymes. At necropsy all five of the dogs that died or were euthanized had moderate periportal or severe pazonal hepatic fatty change; two had duodenal ulceration; and two had pancreatic edema. Of two other clinically normal 5X dogs (out of four euthanized as comparators to the clinically affected dogs), one had slight and one had moderate periportal hepatic fatty change. Drug treatment was discontinued for four dogs in the 5X group. These dogs survived the remaining 14 weeks of the study. On average, the dogs in the 3X and 5X dose groups did not gain as much weight as control dogs. Rate of weight gain was measured (instead of weight loss) because these were young growing dogs. Thalamic vacuolization was seen in three of six dogs in the 3X dose group, five of twelve dogs in the 5X dose group, and to a lesser degree in two unmedicated controls. Diarrhea was seen in all dose groups, including unmedicated controls. In a separate dose tolerance safety study involving a total of six dogs (two control dogs and four treated dogs), firocoxib was administered to four healthy adult Beagle dogs at 50 mg/kg (ten times the recommended daily dose) for twenty-two days. All dogs survived to the end of the study. Three of the four treated dogs developed small intestinal erosion or ulceration. Treated dogs that developed small intestinal erosion or ulceration had a higher incidence of vomiting, diarrhea, and decreased food consumption than control dogs. One of these dogs had severe duodenal ulceration, with hepatic fatty change and associated vomiting, diarrhea, anorexia, weight loss, ketonuria, and mild elevations in AST and ALT. All four treated dogs exhibited progressively decreasing serum albumin that, with the exception of one dog that developed hypoalbuminemia, remained within normal range. Mild weight loss also occurred in the treated group. One of the two control dogs and three of the four treated dogs exhibited transient increases in ALP that remained within normal range.

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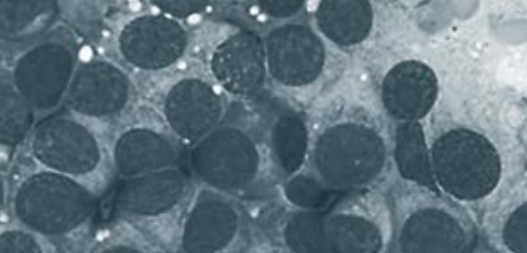
### **Important Safety Information**

As a class, cyclooxygenase inhibitory NSAIDs may be associated with gastrointestinal, kidney or liver side effects. These are usually mild, but may be serious. Pet owners should discontinue therapy and contact their veterinarian immediately if side effects occur. Evaluation for pre-existing conditions and regular monitoring are recommended for pets on any medication, including PREVICOX. Use with other NSAIDs, corticosteroids or nephrotoxic medication should be avoided. Refer to the full Prescribing Information for complete details. See page 44 for product information summary.



**REFERENCES:** 1. Pollmeier M, Toulemonde C, Fleishman C, Hanson PD. Clinical evaluation of firocoxib and carprofen for the treatment of dogs with osteoarthritis. *Vet Rec.* 2006;159(17):547-551. 2. Data on file at Merial.

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# Capsules

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## Of All the Nerve (Blocks)!

Nerve blocks are commonly used in veterinary dentistry. Inadvertent penetration of the globe because of improper technique is an important complication. A 4-year-old Chihuahua experienced transient unilateral vision loss after injection of bupivacaine into the globe during a dental procedure. The operator had attempted bilateral caudal maxillary nerve blocks via an extraoral approach using a 0.2-mL mixture of bupivacaine hydrochloride (0.5%) and epinephrine (1:200 000). For a caudal maxillary nerve block, the needle is inserted along the rostroventral border of the zygomatic arch and directed rostrally toward the opposite nostril. However, in this case, the needle was directed dorsally and into the orbit. Subconjunctival hemorrhage was noted in the left eye immediately following the procedure. Two days later, the dog presented with acute vision loss. Menace response was absent, but direct and consensual pupillary light reflexes were intact. A pearlescent multilobulated vitreal opacity, presumed to be anesthetic precipitate, and diffuse hemorrhage were present. The optic nerve was mildly hyperemic. Intraocular pressures were in the high-normal range. The lens capsule and retina were intact. The dog was treated with amoxicillin-clavulanate and carprofen. At 1-week follow-up, vision was apparently normal, menace response was present, and intraocular pressure was in the mid-normal range. The vitreal opacity had resolved, the optic nerve was unchanged, and there were no retinal abnormalities. The authors attributed the temporary vision loss to vitreal opacity and hemorrhage. Extra care should be taken to avoid accidental intravitreal injection when attempting dental nerve blocks, particularly in cats and brachycephalic dogs.

### Commentary

Local dental nerve blocks are becoming more popular to help decrease patient discomfort and, in many cases, the amount of general anesthesia required when painful stimulation occurs. It is important that the person delivering the anesthetic (preferably a veterinarian) is familiar with the anatomy that the tip of the needle may encounter. In this case, the anterior chamber of the eye was inadvertently penetrated.

To avoid such a complication, we do not perform the extraoral caudal maxillary nerve block. Instead, we use the intraoral technique, depositing 0.1-0.3 mL 0.5% bupivacaine hydrochloride with epinephrine (Marcaine, hospira.com) (1 mg/kg) and lidocaine 2% (1 mg/kg) in a 4:1 ratio. (Mixing 0.8 mL of bupivacaine with 0.2 mL of lidocaine in the same tuberculin syringe accomplishes the 4:1 ratio.)

With the dog or cat's mouth opened, palpate the zygomatic arch where it meets the maxilla between the fourth premolar and molar. Direct the needle next to the bone, and advance dorsally 1-3 mm along the caudal aspect of the notch to a level just beyond the second molar distobuccal root tips in the dog and the last molar in the cat. Aspirate the needle, and slowly inject the anesthetic agent.—*Jan Bellows, DVM, DAVDC, DABVP*

### Source

Alessio TL, Krieger EM. Transient unilateral vision loss in a dog following inadvertent intravitreal injection of bupivacaine during a dental procedure. *JAVMA*. 2015;246(9):990-993.

continues





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<sup>1</sup> Reference on file. Bayer HealthCare, Animal Health.

<sup>2</sup> Reference on file. Bayer HealthCare, Animal Health.

<sup>3</sup> Mueller RS, Bergvall K, Bensignor E, et al. (2012). A review of topical therapy for skin infections with bacteria and yeast. *Vet Dermatology*. 23:330-341.

\* Studies were performed using Malaseb® Concentrate Rinse (0.2% Miconazole and 0.2% Chlorhexidine); *Staphylococcus pseudintermedius* (also known as *Staphylococcus intermedius*), *Pseudomonas aeruginosa*, *Malassezia pachydermatis*; The clinical significance of *in vitro* data has not been determined.

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## FOCUS Distortion Control

Circular external fixators are composed of rings or arches interconnected by threaded rods to create a rigid frame. Small, tensioned transfixing wires secure the frame to the bone. Correct anatomic location of the transfixing wires is important to ensure proper fixation and a good surgical outcome. Understanding the effects of radiographic distortion is critical. In this study, 10 radiographic images were taken of 3 circular external fixators with differing intersecting angles (30°, 60°, and 90°) for transfixing wires. The 10 images were obtained by rotating the device through varying degrees from parallel with the central x-ray beam (10°-80°). For all 3 devices, distortion was greatest when transfixing wires were at smaller angles of rotation or farthest from the

x-ray table. Likewise, at all angles of rotation, the 30° device created the greatest distortion. The authors demonstrated that angle and distance from the table affected distortion. This could mislead the interpreter and lead to unnecessary surgical adjustments, anesthesia time, and repeated radiography. Placement of the fixator in the center of the x-ray beam with the wire intersection as close to the table as possible can best reduce distortion artifact.

### Commentary

External skeletal fixators (ESFs) are versatile devices used in orthopedic practice to treat conditions such as fractures and limb deformities. The components are metallic, which makes radiographic

assessment of bones and the fixation extremely challenging. It is important to consider the position of the device and angle of the radiographic beam because distortion can be substantial, as this study shows. The radiographic beam should be centered on the area of interest and positioned 0° or 90° orthogonal to the fixation in order to minimize artifacts. This may require several different views along various aspects of a long bone or fixator, at various obliquities, to fully appreciate each fixation element in an ESF construct.—*Jason Bleedorn DVM, DACVS*

### Source

Secrest S, Nagy J, Kneller S. Radiographic distortion artifact of circular external fixators. *JAAHA*. 2015; 51(3):143-147.

## Feline USG: When to Worry



Urine specific gravity (USG) is a useful, practical tool for evaluating kidney function in cats. Previous studies have suggested that healthy cats should have a USG >1.035, but no large-scale studies have been conducted. This prospective cross-sectional study evaluated the USG of 1040 healthy cats that were presented to primary practices, and the environmental factors (eg, age, gender, diet, collection time, lifestyle) that may affect USG. The results confirmed that 88% of adult cats and 92% of young (<6 months old) cats had USG ≥1.035, which led authors to conclude that a USG >1.035 should be expected in apparently healthy cats. Most environmental factors minimally affected USG, which decreased slightly with increasing age, was lower in females, higher in unfasted cats, lower in cats with increasing drinking avidity, and higher when measured at reference laboratories than in-house with refractometers. Sampling time did not affect USG. Dietary changes implemented to reduce the USG by increasing the moisture content of the diet were only slightly effective, and only in females. The authors recommend monitoring the USG of cats when dietary changes are made to determine efficacy. The authors recommend that cats ≥9 years of age that have a USG <1.035 be further evaluated to determine the cause of the low USG; these cats were more likely to have subclinical disease identified than were younger cats with USG <1.035.

### Global Commentary

Assessment of USG is a simple diagnostic test, invaluable in interpreting the presence of azotemia and assessing the cat's urine concentrating ability. This study confirms that most (88%) healthy cats (irrespective of age) produce a USG >1.035. Importantly, investigation of adults with a USG <1.035 revealed an underlying disease in 38%, and in an even higher proportion of cats ≥9 years of age. These results emphasize the importance of not ignoring a USG <1.035 in spot urine samples. Importantly, different refractometers yielded significantly different results, and other studies have also shown that feline-specific refractometers are unnecessary and less reliable.<sup>1</sup> This study showed the importance of spot-checking feline USG, and it is likely that serial measurements of USG in individual cats over time (especially those ≥9 years old) would yield even more valuable results in the future.—*Andy Sparkes, BVetMed, PhD, DECVIM-MRCVS*

### Reference

1. Tvedten HW, Ouchterlony H, Lilliehöök IE. Comparison of specific gravity analysis of feline and canine urine, using five refractometers, to pycnometric analysis and total solids by drying. *N Z Vet J*. 2015;63(5):254-259.

### Source

Rishniw M, Bicalho R. Factors affecting urine specific gravity in apparently healthy cats presenting to first opinion practice for routine evaluation. *J Feline Med Surg*. 2015;17(4):329-337.

## Stemming the Tide of CCL?

Interest in adjunctive treatments for canine cranial cruciate ligament (CCL) tears is driven by lack of ideal long-term surgical outcomes. One promising new approach is mesenchymal stem cell (MSC) therapy. MSCs accelerated healing of transected ligaments in animal models. Fresh, whole bone marrow cells (BMCs) may have greater effects because of their ability to differentiate into the target tissue type. BMCs would also be more practical clinically. This study evaluated the engraftment potential of autologous BMCs injected intra-articularly in dogs with natural CCL tears and examined whether PKH26 red fluorescent dye labeling is a safe, effective way to track canine BMCs.

Bone marrow was harvested from 7 client-owned dogs presenting for surgical CCL repair. Cells were labeled with PKH26 and, following synovial fluid aspiration, injected into the stifle. Detection rate remained low, however, with labeled cells found in 3/7 dogs and small numbers of engrafted cells in these cases. Future studies should address whether injection of higher numbers of BMCs is safe and more effective. Although the clinical procedure tested was practical and safe, results

imply that application of MSCs may prove superior to BMCs for engraftment and cell tracking after PKH26 labeling.

### Commentary

The use of stem cells has gained widespread attention with clinical uses from cardiovascular disease to arthritis. Although researchers have investigated source, dose, viability of cells, and effects in various diseases, prospective studies documenting efficacy in canine orthopedic disease are lacking. This study tracked stem cells delivered into canine stifles and found that a small number of cells did engraft on the injured CCL. Future studies could explore the use of stem cells in cases of partial CCL tears in which force plate and gait analysis could be used to measure improvement.—*Brenda Salinardi, DVM, MS, DACVS*

### Source

Linon E, Spreng D, Rytz U, Forterre S. Engraftment of autologous bone marrow cells into the injured cranial cruciate ligament in dogs. *VET J* 2014;202(3):448-454.

## Optimal Gastric Acid Suppression in Dogs

In critically ill dogs, GI bleeding is a common complication with many causes, including NSAID toxicosis, liver failure, and GI neoplasia. Treatment includes acid-suppressant administration to increase the gastric pH. Famotidine works within hours compared to a proton pump inhibitor (PPI) such as pantoprazole, which takes several days to reach peak effect. Many veterinarians administer the rapidly acting famotidine in the first few days in combination with the slower-acting pantoprazole to critically ill dogs with high risk for GI bleeding, but there is no evidence demonstrating an advantage with this combination. Many pharmacologists argue that combination therapy may interfere with the efficacy of the PPI. In this randomized crossover study, gastric pH changes over a 3-day period were compared in healthy dogs ( $n = 12$ ) given IV famotidine with pantoprazole or pantoprazole alone. All treatments were dosed at 1 mg/kg IV q12h for 3 days, and continuous intragastric pH monitoring was performed. In humans, mean percentage time (MPT) intragastric pH  $\geq 3$  is the ideal baseline for GI ulceration healing; MPT  $\geq 4$  is ideal for healing of gastroesophageal reflux lesions. No significant differences were found between the MPT that gastric pH was  $\geq 3$  and  $\geq 4$  between the 2 groups in this study. The monotherapy group also remained above target pH levels

for longer periods than the combination-therapy group. There appears to be no advantage to giving famotidine in addition to pantoprazole for increasing gastric pH.

### Commentary

PPIs such as pantoprazole reach peak effect after 4 days of therapy, which is why many veterinarians co-administer famotidine during the first several days of treatment. The work presented here shows that there is no difference in acid suppression between PPI monotherapy and combined treatment with pantoprazole and famotidine. Practitioners are also reminded that previous research has shown that q12h PPI administration can provide superior acid suppression compared to q24h dosing. This research adds to what is known about optimal acid suppression therapy in dogs, moving our profession toward an understanding of how to best treat dogs with GI bleeding.—*Julie M. Walker, DVM, DACVECC*

### Source

Tolbert MK, Odunayo A, Howell RS, Peters EE, Reed A. Efficacy of intravenous administration of combined acid suppressants in healthy dogs. *JVIM*. 2015; 29(2):556-560.

continues

# Bile, Bacteria, & Bactibilia

In dogs, bacterial cholecystitis and bactibilia are important differentials for patients presenting with signs of biliary tract disease. This report examined 10 bacterial cholecystitis or bactibilia cases and compared them to 30 control dogs with hepatobiliary disease without bactibilia or cholecystitis. Data examined included signalment, history, clinicopathologic data, ultrasound findings, cultures, surgical observations, histopathology, treatment, and outcomes.

Although no examination or clinicopathologic variable was specific to bacterial cholecystitis or bactibilia, immobile biliary sludge, identified in 7 case dogs but no control dogs, was 70% sensitive and 100% specific for bactibilia diagnosis. Ultrasound-guided cholecystocentesis to collect samples for cytology and bacteriologic culture was performed in all 40 dogs. This procedure had no associated complications and assisted in confirming diagnosis and guiding appropriate antimicrobial therapy. Four case dogs were managed medically with ursodeoxycholic acid and extended antimicrobial treatment periods. Serum chemistry panel and bile culture were repeated monthly. Clinical signs and clinicopathologic changes improved in 2 of 4 treated dogs before resolution of bactibilia, which took 4 to 9 months. All medically managed dogs had good outcomes. Surgical cholecystectomy also provided good outcomes. Inflammatory bowel disease was present histologically in 3/4 case dogs for which intestinal biopsies were obtained; unlike in cats, no previous association between cholangitis and IBD in dogs has been noted.

## Commentary

In this study, enteric bacteria were the predominant type isolated (*Escherichia coli* as most common), with 2 anaerobic isolates identified. The high incidence of antimicrobial drug resistance found with previous antimicrobial treatment, especially in *Enterococcus* spp isolates, is concerning. The combination of biliary ultrasonography and ultrasound-guided bile sample collection may adequately screen for bactibilia in dogs with hepatobiliary disease, particularly if immobile biliary sludge is identified. In addition, repeated bacteriologic bile culture to monitor response to medical management can be important in these patients, particularly because resolution of clinical signs and improvement of clinicopathologic variables were noted before bactibilia resolution. In cases managed surgically, the immediate postoperative mortality rate was similar to previous reports (22%-40%).—*Ana Costa, DVM, MS, DACVIM*

## Source

Lawrence YA, Ruaux CG, Nemanic S, Milovancev M. Characterization, treatment, and outcome of bacterial cholecystitis and bactibilia in dogs. *JAVMA*. 2015;246(9):982-989.

continues

## NexGard® (afoxolaner) Chewables

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

### Description:

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

### Indications:

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

### Dosage and Administration:

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

### Dosing Schedule:

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

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

### Flea Treatment and Prevention:

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

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

### Tick Treatment and Control:

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

### Contraindications:

There are no known contraindications for the use of NexGard.

### Warnings:

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

### Precautions:

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 afoxolaner; 200 administered active control), no serious adverse reactions were observed with NexGard.

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

**Table 1: Dogs With Adverse Reactions.**

	Treatment Group			
	Afoxolaner		Oral active control	
	N <sup>1</sup>	% (n=415)	N <sup>2</sup>	% (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

<sup>1</sup>Number of dogs in the afoxolaner treatment group with the identified abnormality.

<sup>2</sup>Number of dogs in the control group with the identified abnormality.

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

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](http://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 <http://www.fda.gov/AnimalVeterinary/SafetyHealth>.

### Mode of Action:

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

### Effectiveness:

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

In a 90-day US field study conducted in households with existing flea infestations of varying severity, the effectiveness of NexGard against fleas on the Day 30, 60 and 90 visits compared with baseline was 98.0%, 99.7%, and 99.9%, respectively. Collectively, the data from the three studies (two laboratory and one field) demonstrate that NexGard kills fleas before they can lay eggs, thus preventing subsequent flea infestations after the start of treatment of existing flea infestations.

In well-controlled laboratory studies, NexGard demonstrated >97% effectiveness against *Dermacentor variabilis*, >94% effectiveness against *Ixodes scapularis*, and >93% effectiveness against *Rhipicephalus sanguineus*, 48 hours post-infestation for 30 days. At 72 hours post-infestation, NexGard demonstrated >97% effectiveness against *Amblyomma americanum* for 30 days.

### Animal Safety:

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

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

### Storage Information:

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

### How Supplied:

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

NADA 141-406, Approved by FDA

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

Made in Brazil.

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1050-4493-03  
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A Division of Merial



# Killing fleas and ticks can be just **this easy.**

With NexGuard® (afoxolaner), flea and tick control is convenient for pet owners since dogs love taking the soft, beef-flavored chew.<sup>1</sup>

**POWERFUL** flea and tick killing all month long

**CONVENIENT** monthly dosing owners are used to

**EASY** for owners to give<sup>1</sup> and for veterinarians to dispense



Prescription only with anti-diversion technology



<sup>1</sup>Data on File at Merial.

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**IMPORTANT SAFETY INFORMATION:** For use in dogs only. The most common adverse reaction is vomiting. Other adverse reactions reported are dry/flaky skin, diarrhea, lethargy, and anorexia. The safe use of NexGuard in pregnant, breeding, or lactating dogs has not been evaluated. Use with caution in dogs with a history of seizures.

See page 50 for product information summary.

## Making the (Tumor) Grade



Surgical margins 2-3 cm wide and 1 tissue plane deep are typically recommended to create a histologically tumor-free margin (HTFM) and prevent local recurrence (LR) of canine mast cell tumors (MCTs). However, interpretation of how HTFM correlates with LR risk is difficult. The histologic safety margin (HSM), used for basal cell carcinoma in human oncology, is defined as minimum distance from visible tumor edge to closest resection margin that could be determined microscopically for LR prevention. The purpose of this retrospective study was to determine the HSM of low- vs high-grade MCTs in dogs and its association with recurrence rates. Medical records for 73 dogs with 90 grade II and III MCTs were included. Signalment, tumor size and location, treatment, and LR (if applicable) were noted. Tumor specimens were examined, measured for margins, and classified as either low-grade ( $n = 51$ ) or high-grade ( $n = 39$ ) using a 2-tier grading system. The only significant association with LR risk on multivariable analysis was tumor grade: rate of LR for high-grade tumors (35.9%) was significantly higher than that for low-grade tumors (3.9%). No association was found between HTFM size and LR, so the HSM for canine MCT could not be determined. Twenty-nine percent of the low-grade tumors had HTFM  $\leq 3$  mm; none of these recurred. The authors concluded that narrow ( $\leq 3$  mm) margins may be adequate for surgical treatment of low-grade MCT but that high-grade tumors have high recurrence risk regardless of HTFM width.

### Global Commentary

This study suggests that high-grade tumors, as defined by Kuipel, et al,<sup>1</sup> have a high chance of recurring regardless of

surgical margins; conversely, low-grade tumors do not. It also adds to the evidence base that the Kuipel grading system seems to be robust. This is particularly important, as there is a report that the Kuipel grading system was used accurately on cytological samples in 94% of cases.<sup>2</sup> Thus, there is potential to plan treatment and counsel owners after using a minimally invasive technique.

It should be appreciated, however, that pathologists only look at a fraction of the tissue submitted for histopathology; thus, an accurate idea of which margin has truly been taken is limited. It is therefore sensible for the surgeon to identify the margin of concern in some way and to direct the pathologist to that area before sending the tissue to the pathology laboratory. Finally, a study relating to MCTs recurrence noted that if the surgeon had “strong doubts about the completeness of surgery,” local recurrence was “a frequent but not constant phenomenon.”<sup>3</sup>—*Sue Murphy, BVMS&S, MSc (Clin Onc) DECVIM-CA (Onc), MRCVS*

### References

1. Kuipel M, Webster JD, Bailey KL, et al. Proposal of a 2-tier histologic grading system for canine cutaneous mast cell tumors to more accurately predict biological behavior. *Vet Pathol.* 2011; 48(1):147-155.
2. Scarpa F, Sabattini S, Bettini G. Cytological grading of canine cutaneous mast cell tumours. *Vet Comp Oncol.* 2014.
3. Misdorp W. Incomplete surgery, local immunostimulation, and recurrence of some tumour types in dogs and cats. *Vet Q.* 1987;9(3):279-286.

### Source

Donnelly L, Mullin C, Balko J, et al. Evaluation of histological grade and histologically tumour-free margins as predictors of local recurrence in completely excised canine mast cell tumours. *Vet Comp Oncol.* 2015;13(1):70-76.

# quellin®

(carprofen)

soft chewable tablets

Non-steroidal anti-inflammatory drug  
For oral use in dogs only

#### BRIEF SUMMARY:

Before using quellin soft chewable tablets, please consult the product insert, a summary of which follows:

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

**PRODUCT DESCRIPTION:** quellin (carprofen) is a non-steroidal anti-inflammatory drug (NSAID) of the propionic acid class that includes ibuprofen, naproxen, and ketoprofen.

**INDICATIONS:** quellin is indicated for the relief of pain and inflammation associated with osteoarthritis and for the control of postoperative pain associated with soft tissue and orthopedic surgeries in dogs.

**CONTRAINDICATIONS:** quellin should not be used in dogs exhibiting previous hypersensitivity to carprofen.

**WARNINGS:** Keep out of reach of children. Not for human use. Consult a physician in cases of accidental ingestion by humans. **For use in dogs only.** Do not use in cats. All dogs should undergo a thorough history and physical examination before initiation of NSAID therapy. Appropriate laboratory tests to establish hematological and serum biochemical baseline data prior to, and periodically during, administration of any NSAID should be considered.

**PRECAUTIONS:** As a class, NSAIDs may be associated with gastrointestinal, renal and hepatic toxicity. Effects may result from decreased prostaglandin production and inhibition of the enzyme cyclooxygenase which is responsible for the formation of prostaglandins from arachidonic acid. When NSAIDs inhibit prostaglandins that cause inflammation they may also inhibit those prostaglandins which maintain normal homeostatic function. These antiprostaglandin effects may result in clinically significant disease in patients with underlying or pre-existing disease more often than in healthy patients. Carprofen is an NSAID, and as with others in that class, adverse reactions may occur with its use. The most frequently reported effects have been gastrointestinal signs. Events involving suspected renal, hematologic, and neurologic, dermatologic, and hepatic effects have also been reported. Concomitant use of carprofen with other anti-inflammatory drugs, such as other NSAIDs or corticosteroids, should be avoided because of the potential increase of adverse reactions, including gastrointestinal ulcerations and/or perforations. Carprofen is not recommended for use in dogs with bleeding disorders, as safety has not been established in dogs with these disorders. The safe use of carprofen in animals less than 6 weeks of age, pregnant dogs, dogs used for breeding purposes, or in lactating bitches has not been established.

#### ADVERSE REACTIONS:

During investigational studies for the caplet formulation with twice-daily administration of 1 mg/lb., no clinically significant adverse reactions were reported. Some clinical signs were observed during field studies which were similar for carprofen caplet and placebo treated dogs. Incidences were observed in both groups: vomiting (4%), diarrhea (4%), changes in appetite (3%), lethargy (1.4%), behavioral changes (1%), and constipation (0.3%).

For a copy of the Material Safety Data Sheet (MSDS) or to report adverse reactions call Bayer Veterinary Services at 1-800-422-9874. For consumer questions call 1-800-255-6826.

ANADA 200-555 Approved by FDA

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Bayer HealthCare LLC, Animal Health Division,  
PO Box 390, Shawnee Mission, KS 66201

March 2015

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BAY070115

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quellin® (carprofen) soft chewable tablets



# quellin.® (carprofen)

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- Easy for dogs to chew
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**quellin® is indicated for the relief of pain and inflammation associated with osteoarthritis and for the control of postoperative pain associated with soft tissue and orthopedic surgeries in dogs.**



**CAUTION:** Federal law restricts this drug to use by or on the order of a licensed veterinarian. **WARNINGS:** Keep out of reach of children. Not for human use. Consult a physician in cases of accidental ingestion by humans. **For use in dogs only.** Do not use in cats. All dogs should undergo a thorough history and physical examination before initiation of NSAID therapy. Appropriate laboratory tests to establish hematological and serum biochemical baseline data prior to, and periodically during, administration of any NSAID should be considered.

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QL151575

## The Calm *During* the Storm

Noise sensitivities and phobias, especially thunderstorm phobias, are common in dogs. In addition to attention-seeking behaviors, signs include panting, shaking, salivating, hiding, and losing control of the bladder or bowels. Treatment includes behavior modification, homeopathic preparations, botanical extracts, body wraps, and pheromones. In addition, sedatives and/or tranquilizers, tricyclic antidepressants, benzodiazepines,  $\alpha_2$ -agonists, selective serotonin reuptake inhibitors, and serotonin 2A antagonist and reuptake inhibitors have been used successfully to treat thunderstorm phobias. Alternative treatments (eg, acupuncture, herbal medications, homeopathy, nutraceuticals) are popular among clients, who perceive few adverse effects. L-theanine, an amino acid found in green tea, increases the inhibitory neurotransmitter gamma amino butyric acid along with brain serotonin and dopamine levels. Peak blood or liver and CNS concentrations occur 1 and 5 hours after oral administration in animals, respectively.

Nutraceutical supplement Anxitane (virbacvet.com) comprises a 99.95% pure active form of L-theanine (*N*-ethyl-L-glutamine). Owners of 18 dogs completed questionnaires evaluating 11 typical behavior manifestations of storm anxiety before starting treatment (baseline). Dogs then began q12h Anxitane treatment, and owners completed the same questionnaire for each subsequent storm ( $n \geq 5$ ) as well as an exit evaluation. L-theanine decreased severity of dogs' global anxiety during storms, reduced

time for return to baseline normal behavior after storms, and diminished the most commonly reported manifestations of hiding, following people, pacing, panting, and trembling. Owner satisfaction with treatment was high (94%). L-theanine may be an alternative treatment or adjunct for thunderstorm phobias in dogs. *Virbac Animal Health provided educational funding and nutraceutical supplement for the study.*

### Commentary

The use of nutraceuticals in veterinary medicine is extremely popular. Clients prefer medications with few adverse effects, although these products generally lack substantial evidence confirming efficacy. This study shows that L-theanine may be useful in treating thunderstorm phobia because it appeared to lessen the severity of clinical signs. It is important to note that it did not eradicate the phobic behaviors. In addition, this study had a small sample size and was not placebo-controlled. These data could be a stepping stone for further prospective randomized and double-blinded studies to evaluate use of this amino acid as a solo or adjunctive treatment in thunderstorm phobias. At the very least, the use of this amino acid is safe and was without serious recourse in this study.—*Heather Troyer, DVM, DABVP, CVA*

### Source

Pike AL, Horwitz DF, Lobprise H. An open label prospective study of the use of L-theanine (Anxitane) in storm sensitive client owned dogs. *J VET BEHAV.* 2015;10(4):324-331.

**These data could be a stepping stone for further prospective randomized and double-blinded studies.**

continues

## Osurnia®

(florfenicol-terbinafine-betamethasone acetate)

### Otic gel

Antibacterial, antifungal, anti-inflammatory

### For Otic Use in Dogs Only

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

#### Caution:

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

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

**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 corticosteroids has been associated with adrenocortical suppression and iatrogenic hyperadrenocorticism in dogs. Use with caution in dogs with impaired hepatic function. The safe use of OSURNIA in dogs used for breeding purposes, during pregnancy, or in lactating bitches, has not been evaluated.

**Adverse Reactions:** The most common adverse reactions 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 were Elevated Alkaline Phosphatase, Vomiting, and Elevated AST, ALT, ALP\* \*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.

To report suspected adverse drug events, contact Elanco Animal Health at 1-800-332-2761. For additional information about adverse drug experience reporting for animal drugs, contact the FDA at 1-888-FDA-VETS or <http://www.fda.gov/AnimalVeterinary/SafetyHealth>. For technical assistance, contact Elanco Animal Health at 1-800-332-2761.

#### 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). 159 dogs were treated with OSURNIA and 76 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.

NADA # 141-437, Approved by FDA  
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**Manufactured for:** Novartis Animal Health US, Inc., Greensboro, NC 27408 USA  
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# Treating otitis externa just got easier.

Just two doses per ear,  
dosed one week apart

done.

The simple treatment for otitis externa\*, with easy application.

- Just two doses per ear, dosed one week apart
- Same dose for every dog
- Single-dose tube with soft, flexible tip is gentle on a dog's ears
- Easy application may lead to better compliance

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**NEW**

**Osurnia**<sup>®</sup> 

(florfenicol • terbinafine • betamethasone acetate)

### Important Safety Information

OSURNIA<sup>®</sup> (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 on page 54 for additional information.

\*Associated with susceptible strains of bacteria (*Staphylococcus pseudintermedius*) and yeast (*Malassezia pachydermatis*).

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**Elanco**

## Tympanometry: We're All Ears

Examination of the tympanic membrane, bullae, and Eustachian tube can be difficult without advanced imaging. Tympanometry is a noninvasive way to examine middle ear functionality through measurement of reflected sound energy with varying atmospheric pressure applied in the external ear canal. Tympanometry, also known as impedance audiometry, is widely used in human medicine but previously has been too costly for widespread veterinary use. This study evaluated the feasibility of using a lower-cost handheld tympanometer in conscious dogs ( $n = 16$ ) to evaluate the tympanum. These dogs showed no evidence of otitis before testing. With each dog in a standing position, ears were cleaned, then a handheld tympanometer probe tip with an extender adapter was placed into the vertical canal to create a seal. Of 16 dogs, 13 allowed both ears to be examined, 2 only allowed 1 ear to be examined, and 1 dog resisted examination of both ears. Repeated otoscopic examinations confirmed no evidence of otitis in the 3 resisting dogs. Peak compliance pressure, gradient, and ear canal volume were measured. Repeated tests in compliant dogs showed good repeatability. Future studies of dogs with otic disease are needed to confirm the clinical utility of this device.

### Commentary

It can often be difficult to diagnose otitis media in a dog, and not every client can afford a CT scan. Tympanometry may be the tool we need to evaluate the middle ear without advanced imaging. Although this study demonstrated that most dogs tolerate it, the technique has not yet been validated as a means for differentiating dogs with otitis media vs otitis externa. If the authors are able to demonstrate this in future research, it offers significant promise.—*William Oldenhoff, DVM, DACVD*

### Source

Strain GM, Fernandes AJ. Handheld tympanometer measurements in conscious dogs for the evaluation of the middle ear and auditory tube. *Vet Dermatol.* 2015;26(3):193-e40.

## Viral Co-infection in Bacterial Pneumonia



Bacterial pneumonia (BP) is caused by bacterial infection and has a complex pathogenesis. This study investigated the role of respiratory viral infection in canine BP. Client-owned dogs diagnosed with BP ( $n = 20$ ) were included in this prospective observational study. Dogs diagnosed with *Bordetella bronchiseptica* tracheobronchitis ( $n = 13$ ) and showing signs for >30 days served as controls for virus analysis. Thoracic radiographs, hematology, serum chemistry, serum C-reactive protein, blood gas analysis, and fecal analysis were performed on all dogs. Airway samples were collected via bronchoalveolar lavage or transtracheal wash for cytology, aerobic and anaerobic culture, *Mycoplasma* spp culture, and PCR analysis. PCR screening was conducted for canine parainfluenza virus (CPIV), canine adenovirus type 2, canine herpesvirus, canine respiratory coronavirus (CRCoV), canine influenza virus, canine pneumovirus, canine distemper virus, *Mycoplasma* spp, and *B bronchiseptica*. In dogs with BP, CPIV and CRCoV were detected in 7/20 and 1/20 of dogs, respectively. Respiratory viruses were not detected in control dogs. Dogs with bacterial and viral co-infections were significantly heavier and tended to be younger—although not statistically significant—than those without viral co-infection. Clinical findings, arterial blood gas analysis, hematology, and respiratory sample cytology did not differ significantly when BP was accompanied by viral infection, which suggests that viral co-infection did not increase illness severity. Respiratory viruses, primarily CPIV, may play a role in BP pathogenesis but do not necessarily affect clinical course.

### Global Commentary

Airway samples from dogs with suspicion of BP should be submitted for PCR (ie, *B bronchiseptica*, *Streptococcus equi*, *Mycoplasma* spp) and bacterial culture susceptibility testing. However, viral PCR screening should not be routinely performed. In fact, based on these findings, respiratory viruses might predispose to development of secondary bacterial infections; however, they are usually self-limiting and of minor clinical relevance. Treatment includes supportive care (eg, oxygen therapy, sterile saline nebulization followed by coupage, mucolytics, bronchodilators, IV fluids) associated with antimicrobials (chosen on susceptibility testing of isolates or empiric treatment based on positive PCR results). Vaccinations are available for some causal agents to limit infection severity. Prevention strategies should be planned in shelters to decrease morbidity and ease of transmission.—*Alice Tamborini, DVM, MRCVS, DECVIM-CA (Internal Medicine)*

### Source

Viitanen SJ, Lappalainen A, Rajamäki MM. Co-infections with respiratory viruses in dogs with bacterial pneumonia. *JVIM.* 2015;29(2):544-551.

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## Meloxicam—For the Birds?

The selective COX-2 inhibitor meloxicam is commonly prescribed for extralabel use in companion birds because of its availability in oral and injectable forms at useful concentrations. This study assessed potential adverse effects of oral meloxicam in Hispaniolan Amazon parrots (*Amazona ventralis*) at doses previously identified as therapeutic. Twelve healthy parrots were assigned to receive either meloxicam oral suspension (1.6 mg/kg PO q12h) with 2.5 mL tap water ( $n = 8$ ) or the equivalent volume of tap water only ( $n = 4$ ) for 15 days. CBC, serum chemistry analysis, and clotting times were measured, as well as *N*-acetyl- $\beta$ -D-glucosaminidase (NAG) activity as a marker of renal damage. Urinalysis and urine NAG activity were assessed, and feces were checked for occult blood. Treated birds had significant increases in white blood cells (WBCs) and decreases in packed cell volume (PCV) after treatment. PCV in treated birds was significantly lower than in the control group; however, WBC counts and PCV for all birds remained within the reference range throughout the study. There were no effects of treatment on clotting times, uric acid concentration, serum NAG activity, urinalysis variables, or fecal occult blood. Although no clinically relevant changes were seen secondary to meloxicam treatment in these healthy parrots, additional studies are

needed, and patients should be evaluated for organ dysfunction before use.

### Commentary

Pharmacokinetic studies on avian and exotic pets are a much needed addition to the peer-reviewed literature as there is much extralabel use, dosage extrapolation, and confusion with metabolic scaling. Meloxicam is the most commonly used NSAID with a variety of applications in pet birds, but despite the many papers evaluating pharmacokinetics and doses in a variety of bird species, little is known about adverse effects. Although this study was done on a small, species-specific number of healthy Amazon parrot cases, and the method of urine sampling and statistics on a small population was questionable, the results help us better understand the lower likelihood of adverse effects when using a higher dose and frequency of meloxicam, thereby resulting in better analgesia for patients.  
—Anthony A. Pilny, DVM, DABVP (*Avian*)

### Source

Dijkstra B, Guzman DS, Gustavsen K, et al. Renal, gastrointestinal, and hemostatic effects of oral administration of meloxicam to Hispaniolan Amazon parrots (*Amazona ventralis*). *AM J VET RES*. 2015;76(4):308-317.

## Fixing Fractures

This retrospective study assessed the impact of stabilization method on complication rate after lateral humeral condylar fracture (LHCF) repair ( $n = 135$ ) in 132 dogs. LHCFs are intra-articular fractures most commonly seen in skeletally immature animals; they are often traumatic in origin. Transcondylar screws inserted in lag fashion is probably the most common method of fixation, with a second fixation point (most commonly using K-wire) to prevent rotation of the lateral fragment around the axis of the screw. Few studies have compared differing surgical treatments of LHCF. Surgical LHCF repair methods in this study of dogs included transcondylar screw and supracondylar K-wires ( $n = 61$ ), transcondylar screw plus supracondylar screw ( $n = 13$ ), and transcondylar screw plus lateral epicondylar plate ( $n = 61$ ). Major complications were seen significantly more frequently with transcondylar screw and supracondylar K-wire fixation than with stabilization using supracondylar screws or lateral epicondylar plates. Dogs with major complications were significantly more likely to have poor outcomes. Although an increase in anesthesia time led to an increased rate of postoperative infection, no association was seen between duration of anesthesia and fixation method.

Interestingly, no correlation was found between accuracy of reduction and long-term outcome. More studies are needed to clarify the effects of age, weight, and postoperative antibiotic usage on outcome of LHCF repair.

### Commentary

Humeral condylar fractures are articular fractures that are challenging to repair and have a high complication rate. The most common method of fixation of lateral humeral condylar fractures is use of a transcondylar screw in lag fashion and placement of an anti-rotational pin. This study showed a lower complication rate when a supracondylar screw or lateral epicondylar plate was used instead of a pin. Use of a screw or plate instead of a pin should be considered, particularly in dogs that have confounding factors such as supracondylar comminution or evidence of incomplete ossification of the humeral condyle.  
—Brenda Salinardi, DVM, MS, DACVS

### Source

Perry KL, Bruce M, Woods S, Davies C, Heaps LA, Arthurs GI. Effect of fixation method on postoperative complication rates after surgical stabilization of lateral humeral condylar fractures in dogs. *VET SURG*. 2015;44(2):246-255.

# Right Angle— or Wrong Angle

Angular limb deformity of the femur is an important characteristic of developmental patellar luxation, particularly in large-breed dogs. Femoral varus and valgus are associated with medial and lateral patellar luxation, respectively. A radiographic measurement of varus, the anatomic lateral distal femoral angle (a-LDFA) is the angle between the anatomical proximal femoral axis (a-PFA) and the condylar axis. Different a-PFA methods vary by landmark definitions. This cadaveric radiographic study compared radiographic measurement repeatability and reproducibility for 4 a-PFA methods and to determine a-LDFA agreement within and between these methods at 3 increasing angles of distal femoral elevation. All images were analyzed by 2 clinicians, with good inter-observer agreement. Median a-LDFA increased significantly with increasing femoral elevation by all a-PFA methods, and the choice of method affected the measured a-LDFA at all elevations. Combined, these differences could result in errors of  $\pm 2.6^\circ$ , which could affect decisions regarding clinical intervention; however, it is not possible with these results to determine which a-PFA method is most valid.

## Commentary

Femoral deformity develops secondary to patellar luxation in growing dogs. Failure to recognize this bone deformity may contribute to surgical correction failure. Conventional radiography can be used in cases with varus or valgus deformity; however, as shown in this study, it is important to ensure the femur is positioned  $90^\circ$  orthogonal to the radiographic beam. This is a common oversight in clinical practice with inadequate extension of the hips, particularly in cases with concurrent hip dysplasia or arthritis. This can be overcome by using horizontal beam radiography to obtain a true cranio-caudal view of the femur. The presence of femoral torsion, however, requires axial radiographs or CT for assessment. Ultimately, accurate assessment of the limb axis and joint angles is critical for complete patient assessment, determination of a surgical plan, and successful corrective osteotomy.—*Jason Bleedorn, DVM, DACVS*

## Source

Miles JE, Mortensen M, Svalastoga EL, Eriksen T. A comparison of anatomical lateral distal femoral angles obtained with four femoral axis methods in canine femora. *Vet Comp Orthop Traumatol.* 2015;28(3):193-198.

continues

NADA 141-213, Approved by FDA

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**Warning:** Repeated use of meloxicam in cats has been associated with acute renal failure and death. Do not administer additional injectable or oral meloxicam to cats. See Contraindications, Warnings, and Precautions for detailed information.

**Description:** Meloxicam is a non-steroidal anti-inflammatory drug (NSAID) of the oxicam class. Each milliliter of Metacam Oral Suspension contains meloxicam equivalent to 0.5 mg/mL or 1.5 mg/mL and sodium benzoate (1.5 milligrams) as a preservative. The chemical name for Meloxicam is 4-Hydroxy-2-methyl-N-(5-methyl-2-thiazolyl)-2H-1,2-benzothiazine-3-carboxamide-1,1-dioxide. The formulation is a yellowish viscous suspension with the odor of honey.

**Indications:** Metacam Oral Suspension is indicated for the control of pain and inflammation associated with osteoarthritis in dogs.

**Contraindications:** Dogs with known hypersensitivity to meloxicam should not receive Metacam Oral Suspension. Do not use Metacam Oral Suspension in cats. Acute renal failure and death have been associated with the use of meloxicam in cats.

**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. For oral use in dogs only. As with any NSAID, all dogs should undergo a thorough history and physical examination before the initiation of NSAID therapy. Appropriate laboratory testing to establish hematological and serum biochemical baseline data is recommended prior to and periodically during administration. Owner should be advised to observe their dog for signs of potential drug toxicity and should be given a client information sheet about Metacam.

**Precautions:** The safe use of Metacam Oral Suspension in dogs younger than 6 months of age, dogs used for breeding, or in pregnant or lactating dogs has not been evaluated. Meloxicam is not recommended for use in dogs with bleeding disorders, as safety has not been established in dogs with these disorders. As a class, cyclooxygenase inhibitory NSAIDs may be associated with gastrointestinal, renal and hepatic toxicity. Sensitivity to drug-associated adverse events varies with the individual patient. Dogs that have experienced adverse reactions from one NSAID may experience adverse reactions from another NSAID. Patients at greatest risk for renal toxicity are those that are dehydrated, on concomitant diuretic therapy, or those with existing renal, cardiovascular, and/or hepatic dysfunction. Concurrent administration of potentially nephrotoxic drugs should be carefully approached. NSAIDs may inhibit the prostaglandins that maintain normal homeostatic function. Such anti-prostaglandin effects may result in clinically significant disease in patients with underlying or pre-existing disease that has not been previously diagnosed. Since NSAIDs possess the potential to induce gastrointestinal ulcerations and/or perforations, concomitant use with other anti-inflammatory drugs, such as NSAIDs or corticosteroids, should be avoided. If additional pain medication is needed after administration of the total daily dose of Metacam Oral Suspension, a non-NSAID or non-corticosteroid class of analgesia should be considered. The use of another NSAID is not recommended. Consider appropriate washout times when switching from corticosteroid use or from one NSAID to another in dogs. The use of concomitantly protein-bound drugs with Metacam Oral Suspension has not been studied in dogs. Commonly used protein-bound drugs include cardiac, anticonvulsant and behavioral medications. The influence of concomitant drugs that may inhibit metabolism of Metacam Oral Suspension has not been evaluated. Drug compatibility should be monitored in patients requiring adjunctive therapy.

**Adverse Reactions:** Field safety was evaluated in 306 dogs.<sup>1</sup> Based on the results of two studies, GI abnormalities (vomiting, soft stools, diarrhea, and inappetence) were the most common adverse reactions associated with the administration of meloxicam. The following adverse events are based on post-approval adverse drug experience reporting. Not all adverse reactions are reported to FDA/CVM. It is not always possible to reliably estimate the adverse event frequency or establish a causal relationship to product exposure using these data. The following adverse events are listed in decreasing order of frequency by body system.

**Gastrointestinal:** vomiting, anorexia, diarrhea, melena, gastrointestinal ulceration

**Urinary:** azotemia, elevated creatinine, renal failure

**Neurological/Behavioral:** lethargy, depression

**Hepatic:** elevated liver enzymes

**Dermatologic:** pruritus

Death has been reported as an outcome of the adverse events listed above. Acute renal failure and death have been associated with use of meloxicam in cats.

**Information for Dog Owners:** Metacam, like other drugs of its class, is not free from adverse reactions. Owners should be advised of the potential for adverse reactions and should be informed of the clinical signs associated with drug intolerance. Adverse reactions may include vomiting, diarrhea, decreased appetite, dark or tarry stools, increased water consumption, increased urination, pale gums due to anemia, yellowing of gums, skin or white of the eye due to jaundice, lethargy, incoordination, seizure, or behavioral changes. Serious adverse reactions associated with this drug class can occur without warning and in rare situations result in death (see Adverse Reactions). Owners should be advised to discontinue Metacam and contact their veterinarian immediately if signs of intolerance are observed. The vast majority of patients with drug related adverse reactions have recovered when the signs are recognized, the drug is withdrawn, and veterinary care, if appropriate, is initiated. Owners should be advised of the importance of periodic follow up for all dogs during administration of any NSAID.

**Effectiveness:** The effectiveness of meloxicam was demonstrated in two field studies involving a total of 277 dogs representing various breeds, between six months and sixteen years of age, all diagnosed with osteoarthritis. Both of the placebo-controlled, masked studies were conducted for 14 days. All dogs received 0.2 mg/kg on day 1. All dogs were maintained on 0.1 mg/kg oral meloxicam from days 2 through 14 of both studies. Parameters evaluated by veterinarians included lameness, weight-bearing, pain on palpation, and overall improvement. Parameters assessed by owners included mobility, ability to rise, limping, and overall improvement. In the first field study (n=109), dogs showed clinical improvement with statistical significance after 14 days of meloxicam treatment for all parameters. In the second field study (n=48), dogs receiving meloxicam showed a clinical improvement after 14 days of therapy for all parameters; however, statistical significance was demonstrated only for the overall investigator evaluation on day 7, and for the owner evaluation on day 14.<sup>1</sup>

Reference: 1. FOI for NADA 141-213 (Metacam® (meloxicam) 0.5 mg/mL and 1.5 mg/mL Oral Suspension).

Manufactured for:

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St. Joseph, MO 64506 U.S.A.

US Patent 6,184,220

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**IMPORTANT SAFETY INFORMATION: METACAM Oral Suspension is for use in dogs only.** As a class, cyclo-oxygenase inhibitory NSAIDs may be associated with gastrointestinal, kidney, or liver side effects. The most common side effects reported in field studies were vomiting and soft stool/diarrhea. These are usually mild, but may be serious. If side effects occur, dog owners should halt therapy and contact their veterinarian. Dogs should be evaluated for pre-existing conditions and currently prescribed medications prior to treatment with METACAM, then monitored regularly while on therapy. Concurrent use with another NSAID, corticosteroid, or nephrotoxic medication should be avoided or monitored closely. Please refer to the package insert for complete product information or visit [www.metacam.com](http://www.metacam.com). See page 59 for product information summary.



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## Mushrooms & Respiratory Failure

Although many wild mushrooms are harmless, others are potentially toxic. This retrospective case series evaluated 3 dogs with known mushroom ingestion (either witnessed or found following vomiting or gastric lavage) that developed respiratory arrest after presenting to the hospital with vomiting, tremors, and/or ataxia. None of the patients reportedly had access to any other toxin. IV diazepam was administered in 2 dogs, although it was unclear whether it had any clinical efficacy; these dogs recovered uneventfully after intensive supportive care, including manual or mechanical ventilation, IV fluids, and injectable medications. The third dog's owners elected humane euthanasia because of clinical deterioration. Mushroom analysis was performed in only 1 case; however, neurologic or respiratory effects were not associated with mushrooms identified in this case. It was theorized that a previously unidentified or unknown compound or a mushroom type not recovered in the vomitus caused the clinical signs. One mushroom species, *Amanita* spp, is known to contain muscimol, a biologically active GABA analog. GABA stimulation causes respiratory arrest/apnea, and it is thought that a GABAergic

compound was the underlying cause of severe clinical signs in these 3 dogs.

### Commentary

Fungi are the most versatile, largest group of living organisms on earth. They can eliminate soil pollution, be used to treat infections, and produce insecticides. They can taste good, too, but they can impair and kill animals and humans. This article discusses a few things to consider when managing patients suspected of ingesting a poisonous fungus: 1) orogastric lavage may be helpful in recovering and identifying ingested mushrooms (in addition to decontamination); 2) benzodiazepines may contribute to respiratory failure; and, 3) respiratory failure may be reversible. It also reminded me how much more there is to discover in this world.—*Elke Rudloff, DVM, DACVECC*

### Source

Brandin AC, Meola SD, Mazzaferro EM. Respiratory arrest following ingestion of wild mushrooms in 3 dogs (2006-2011). *JVECC*. 2013;23(6):605-609.

## Putting Itraconazole to the Test

Itraconazole is commonly used to treat systemic fungal infections in dogs, but the original (innovator) brand formula can be cost-prohibitive because of long treatment durations. Few data exist regarding the oral bioequivalence of generic and compounded itraconazole. Itraconazole is lipophilic, nearly insoluble in water, and requires an acidic environment for dissolution. Absorption is variable and can only be verified by measuring plasma concentrations, which are not routinely performed. The innovator itraconazole is coated with sugar spheres to increase surface area and solubility. In this randomized, 3-way, 3-period crossover design study, 9 dogs received either innovator, approved human generic itraconazole capsules, or compounded itraconazole made using bulk itraconazole powder. An 8-day washout was observed. Concentration data were analyzed using pharmacokinetics to determine area under the

curve (AUC), peak concentration ( $C_{MAX}$ ), and terminal half-life. Bioequivalence tests were used to compare generic and compounded formulations to the innovator formula.

There was a lack of bioequivalence for both the generic and compounded itraconazole compared to the reference innovator formulation. Average AUC for the generic formulation was higher, the half-life was similar, and the  $C_{MAX}$  was only slightly lower. Although not bioequivalent, it is likely that therapeutic concentrations are possible with the generic formulation. The compounded formulation, in contrast, had low absorption and bioavailability and should not be used.

### Commentary

This is an elegant study designed to address a long-held suspicion that bioavailability of compounded drugs is likely

not equivalent to that of brand-name or generic drugs. Antimicrobials must remain within targeted therapeutic ranges to be effective and to avoid selection for resistant organisms; this study reinforces significant caution in considering compounded antimicrobial medication for clinical patients. At the same time, it supports the use of generic alternatives when cost, dosing logistics, or manufacturing issues prevent the use of brand-name formulations. We should demand more of these studies before being so willing to accept untested (and unregulated) compounded formulations.—*Jonathan Dear, DVM, DACVIM*

### Source

Mawby DI, Whittemore JC, Genger S, Papich MG. Bioequivalence of orally administered generic, compounded, and innovator-formulated itraconazole in healthy dogs. *JVIM*. 2014;28(1):72-77.

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## Different Approaches to Chronic Constipation

A common disease in humans, chronic constipation (CC) is categorized as outlet obstruction constipation, slow transit constipation, or both. Outlet obstruction involves impaired relaxation and coordination of abdominal and pelvic floor muscles during evacuation, and slow transit is defined as prolonged stool transit (>3 days) through the colon. Available pharmacologic agents typically consist of bulk or stimulant laxatives; many patients find these to be dissatisfactory because of inconsistent results. Alternative therapies reviewed in this article included acupuncture, herbal medicine, moxibustion, and massage.

Acupuncture methods include dry acupuncture, electroacupuncture, transcutaneous electroacupuncture, and auricular acupuncture. Dry acupuncture is commonly performed without electrical current on the needles. Electro- and transcutaneous electroacupuncture both use low-level electrical current either on the needles or on electrodes. Several factors influenced the reported efficacy of acupuncture: acupoint group, operative puncture technique, stimulation parameters, and treatment interval. Moxibustion is a traditional Chinese therapy used to stimulate acupoints with burning moxa made from mugwort. The only high-quality study on moxibustion showed no effect on CC. Likewise, although abdominal massage may be appreciated by CC patients, no measurable improvement was reported in several studies. Herbal medicines studied include the laxatives psyllium and *Ficus carica* as well as traditional Chinese herbal combinations for which there are several high-quality, placebo-controlled trials in the literature. Overall, there is good evidence supporting acupuncture and herbal medicine to treat CC, whereas higher-quality studies are needed for massage and moxibustion.

### Commentary

Acupuncture is a useful treatment for various diseases, but small animal gastrointestinal disease is the most conventionally accepted category by Western veterinarians. There are points to aid in the treatment of nausea and diarrhea and to improve motility in conditions involving ileus or constipation. The commonly used point in this article, ST25, is a more difficult point to use in small animals because of the location on the animal's undercarriage. It also requires a deep needle insertion for stimulation that may actually involve puncture of the peritoneum and/or direct bowel stimulation by needle contact; the exact mechanism of action at this point is unknown. This style of acupuncture is not practiced in veterinary medicine because of obvious risk of abdominal infection. Points that are easier to access in small animals, such as ST36, are tolerated and useful for treatment of some GI diseases.—*Heather Troyer, DVM, DABVP, CVA*

### Source

Wang X, Yin J. Complementary and alternative therapies for chronic constipation. *eCAM*. 2015;2015:1-11.

continues

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# An Eye-Opening Look at *Onchocerca lupi*



Human cases of zoonotic filariasis are increasingly being recognized. *Dirofilaria immitis* and *D repens* infect dogs and have been documented to infect humans. *Onchocerca lupi*, the causative agent of canine and feline onchocercosis, was first identified in a wolf from eastern Europe and since then has been recognized in dogs and cats; there have been several reports of human cases. Over a 3-year period, 8 *O lupi* cases were diagnosed in dogs in the United States: 1 in Minnesota, 4 in New Mexico, 2 in Colorado, and 1 in Florida. All dogs were presented for ocular problems and had nodular lesions in and around the eyes. Nodules were removed from the conjunctiva or sclera and contained filarial-like parasites. Five of 8

dogs responded to treatment; 3 relapsed. Molecular diagnostics confirmed the nematodes as *O lupi*; further analysis suggested the presence of a unique *O lupi* haplotype imported from Europe and circulating in the United States. Molecular testing suggested the infection originated in Europe and was imported to the United States.

### Commentary

Rare diseases occur rarely, but they do occur. This paper adds one more thing (ocular nodules) to consider with ocular disease and highlights another potentially emerging zoonotic disease. Because *O lupi* was found in various parts of the United States, this parasite may have established itself endemically across much of the country. With molecular data grouping these cases with *Onchocerca* spp

from Europe and limited genetic variation among US specimens, it was probably relatively recently imported from Europe with an infected dog. Fortunately, this is a relatively treatable issue for affected dogs and, although zoonotic, probably poses limited risk to humans. However, it demonstrates the ongoing clinical challenges of infectious diseases, the need to be vigilant, and the potential for international movement of pathogens along with the largely unrestricted movement of dogs. —*J. Scott Weese, DVM, DVSc, DACVIM*

### Source

Otranto D, Giannelli A, Latrofa MS, et al. Canine infections with *Onchocerca lupi* nematodes, United States, 2011-2014. *Emerg Infect Dis.* 2015;21(5): 868-871. ■ **cb**

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# Dexmedetomidine & Atipamezole

**Martin J. Kennedy, DVM**

**Rebecca A. Johnson, DVM, PhD, DACVAA**

*University of Wisconsin–Madison*

Dexmedetomidine is an  $\alpha_2$ -agonist that produces varying degrees of sedation, muscle relaxation, and analgesia. The duration of sedation is approximately 1 to 3 hours when administered at the recommended IM or IV doses (1-10  $\mu\text{g}/\text{kg}$ ), with IM administration providing longer periods of sedation. These effects are reversed by the  $\alpha_2$ -antagonist atipamezole (0.1-0.3 mg/kg IM), which is available in a 5 mg/mL formulation (Antisedan; zoetisus.com).

## Dexmedetomidine

### Indications

Dexmedetomidine is approved for use in dogs and cats to facilitate physical examination, minor clinical procedures, and as a preanesthetic medication. Dexmedetomidine is also used to provide sedation during emergence delirium from general anesthesia. Constant rate infusions of dexmedetomidine (0.5-3.0  $\mu\text{g}/\text{kg}/\text{h}$  IV) can also provide prolonged sedation for anxious or disorderly inpatients.<sup>1</sup>

### Contraindications & Drug Interactions

Dexmedetomidine should, in general, be reserved for young, healthy patients. Dexmedetomidine has significant negative cardiovascular effects (see **Advantages & Disadvantages**, next page) and is contraindicated in any patient suffering from or having a predilection for cardiovascular disease. There is argument, however, that dexmedetomidine may be beneficial in cats with hypertrophic cardiomyopathy (HCM) showing dynamic left ventricular outflow tract (LVOT) obstruction, where the increase in systemic vascular resistance and decrease in heart rate produced by  $\alpha_2$ -agonists may actually eliminate the LVOT obstruction.<sup>2</sup> Dexmedetomidine is also contraindicated in patients suffering from respiratory disorders, liver disease, kidney disease, shock, severe debilitation, or stress caused by extreme heat, cold, or fatigue.<sup>3</sup> The medication can produce vomiting in dogs and cats following IM administration, so it is also contraindicated when vomiting could be significantly detrimental to the patient (eg, increased intraocular pressure, increased intracranial pressure, increased intragastric pressure). Because  $\alpha_2$ -agonists reduce uterine blood flow and may affect intrauterine pressure, dexmedetomidine is not recommended for use in pregnant animals.

Because of its sedative and analgesic properties, dexmedetomidine can potentiate the effects of other sedatives, induction agents, inhalant anesthetics, and opioids. Administered alone,  $\alpha_2$ -agonists produce minimal respiratory effects in healthy dogs and cats, characterized by a decrease or no change in respiratory rate and minimal change in



1 Oxygen supplementation via face mask to a dog following dexmedetomidine sedation. Hemoglobin saturation, read from the pulse oximeter placed on the lip, is 100% and heart rate is 75 beats per minute.

HCM = hypertrophic cardiomyopathy, LVOT = left ventricular outflow tract

continues

blood gas tension.<sup>4</sup> Nonetheless, significant hypoventilation resulting in hypoxia can occur when  $\alpha_2$ -agonists are administered with other drugs (eg, opioids, ketamine, propofol), so oxygen supplementation is recommended when dexmedetomidine is administered with other drugs (Figure 1, previous page).<sup>5</sup> Supplemental oxygen may prevent hypoxemia but will not prevent respiratory acidosis. Premedication with dexmedetomidine can reduce the amount of anesthetic induction drug required by approximately 30% to 60% and the inhalant anesthetic requirements by approximately 35% to 90%, depending on dose.<sup>3,5</sup> With this in mind, anesthetic induction and maintenance drugs should always be titrated to effect, and patients should be closely monitored throughout the procedure.

Administration of dexmedetomidine results in increased systemic vascular resistance, bradycardia, and a marked decrease in cardiac output.<sup>6</sup> The initial decrease in heart rate is a reflex bradycardia caused by the increase in systemic vascular resistance. The use of anticholinergics before or after administration of dexmedetomidine is controversial. Treatment with anticholinergics before administration of dexmedetomidine prevents bradycardia; however, cardiac output can still be decreased by over 50%, despite normalization of heart rate.<sup>6</sup> Administering an anticholinergic after dexmedetomidine administration increases the risk of dysrhythmias; thus, routine use of anticholinergics concurrently or after treatment with dexmedetomidine is not recommended.<sup>3</sup> If a patient has profound bradycardia (ie, heart rate <40 beats per minute for dogs, <100 beats per minute for cats) following administration of dexmedetomidine, an electrocardiogram should be evaluated to assess rhythm and, if ventricular escape beats are present, atipamezole should be administered.

Advantages & Disadvantages

Dexmedetomidine produces profound sedation and muscle relaxation that facilitates examination, IV catheter placement, diagnostic procedures, and minor surgical procedures (eg, laceration repair, small tissue biopsy). Analgesia provided by  $\alpha_2$ -agonists has been shown to be synergistic with opioids.<sup>7</sup> In addition, premedication with  $\alpha_2$ -agonists attenuates the stress response elicited by surgery.<sup>8,9</sup> The 0.5 mg/mL formulation of dexmedetomidine also allows for smaller volumes to be injected IM, which may be easier to administer to fractious or less cooperative patients.

Dexmedetomidine has a relatively short duration of action, with sedation lasting from 1-3 hours in dogs and cats at the



**2** Second-degree AV block in a dog following dexmedetomidine administration. There are multiple P waves on the electrocardiogram that do not have associated QRS complexes (arrows). Heart rate is 52 beats per minute.

recommended doses, making it ideal for short procedures or when a patient needs to be discharged on the same day as the procedure. Another advantage of dexmedetomidine is that in the event of complications or excessive sedation, its effects can be reversed by atipamezole administration.

The major disadvantage of dexmedetomidine is its cardiovascular effects, limiting its use to young, healthy patients (American Society of Anesthesiologists [ASA] classification status I and II). Even small doses of  $\alpha_2$ -agonists (approximately 1  $\mu$ g/kg) can decrease cardiac output by approximately 50%.<sup>10</sup> The administration of  $\alpha_2$ -agonists commonly results in a biphasic blood pressure response; initially the patient is bradycardic with elevated blood pressure, but with time the systemic vascular resistance may decrease, resulting in hypotension with continued bradycardia.<sup>11</sup> In addition to bradycardia, a variety of dysrhythmias may be observed, including second-degree atrioventricular (AV) block, third-degree AV block, supraventricular or ventricular tachycardia, supraventricular or ventricular precontractions, and ventricular or junctional escape beats (Figure 2).

Cost

Although the cost of dexmedetomidine may be more than for other sedatives (eg, acepromazine), the reduced amount of induction and maintenance drugs required for anesthesia is likely to offset any additional cost incurred by dexmedetomidine use.

AV = atrioventricular

## Atipamezole

### Indications

Atipamezole reverses the sedative, analgesic, and cardiovascular effects of dexmedetomidine. Atipamezole is approved for IM administration in dogs; it has also been used successfully off-label in cats.<sup>12</sup> Atipamezole is typically administered after completion of a minor procedure performed under dexmedetomidine sedation. When dexmedetomidine has been used for premedication, atipamezole can be administered during anesthesia to treat excessive bradycardia and dysrhythmias, or it can be administered after anesthesia if recovery is prolonged. Atipamezole is also indicated during cardiopulmonary resuscitation when the patient has received dexmedetomidine; in this circumstance, it can be administered IV (0.1 mg/kg).<sup>13</sup>

### Contraindications & Drug Interactions

IV administration of atipamezole is usually contraindicated, except for emergency situations. Atipamezole administered IV may result in rapid relaxation of vascular tone, which coupled with bradycardia could result in cardiovascular collapse.<sup>11</sup> Atipamezole is also formulated with the preservative methylparaben, which can cause histamine release leading to hypotension. It has been recommended that atipamezole and anticholinergics not be used concurrently, as both can cause significant increases in heart rate.<sup>14</sup>

### Advantages & Disadvantages

The major advantage of atipamezole is that it can rapidly reverse the sedative and cardiovascular effects of dexmedetomidine, and cardiac output is returned to baseline levels following administration.<sup>6</sup> Atipamezole is highly selective for the  $\alpha_2$ -receptor and does not have some of the adverse effects associated with less selective  $\alpha_2$ -antagonists (eg, tolazoline, yohimbine). Atipamezole also has a wide safety margin when administered IM.<sup>11</sup>

**The major advantage of atipamezole is that it can rapidly reverse the sedative and cardiovascular effects of dexmedetomidine, and cardiac output is returned to baseline levels following administration.<sup>6</sup>**

Atipamezole is approved only for IM use, as IV administration of  $\alpha_2$ -antagonists can result in hypotension, tachycardia, or even cardiovascular collapse. Another disadvantage is that all analgesia and sedation provided by dexmedetomidine will be reversed by atipamezole. Appropriate analgesia (ie, opioids) should be provided for painful procedures; this will help reduce the dose of dexmedetomidine and provide additional pain control if atipamezole is administered.

In addition, there is the potential for re-sedation from the initial dose of  $\alpha_2$ -agonist approximately 30 to 60 minutes after atipamezole because of its short duration of action.

### Cost

Any additional cost associated with atipamezole can be easily justified by its ability to reverse the negative cardiovascular effects of dexmedetomidine. Atipamezole can minimize the time that patients experience significant cardiovascular depression.

### Conclusion

Dexmedetomidine and atipamezole are useful in many veterinary situations involving healthy dogs and cats requiring sedation, muscle relaxation, and analgesia. However, selection should be on an individual patient basis as dexmedetomidine is associated with significant negative cardiovascular effects. ■ **cb**

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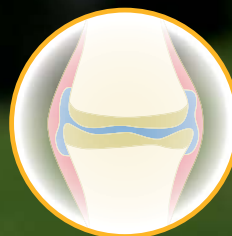
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# Bacterial Pneumonia

Eleanor C. Hawkins, DVM, DACVIM

North Carolina State University

## **P** Profile

### Definition

#### Systems

- Bacterial pneumonia is a lung infection caused by gram-positive or -negative, aerobic or anaerobic bacteria.
  - Mixed infections are common.
  - *Mycoplasma* spp may be involved.
- Bacterial pneumonia caused by atypical organisms such as *Mycobacterium* spp are not considered in this review.

#### Incidence

- The incidence is not known.

#### Geographic Distribution

- Distribution is worldwide.

#### Signalment

##### Species

- Diagnosis is much more common in dogs than in cats.

##### Breed Predisposition

- No primary breed predisposition exists, although underlying disease may have a breed association.

##### Age

- Puppies and kittens are more likely than adults to have bacterial pneumonia from primary infection or underlying viral or congenital causes (eg, cleft palate, megacystophagus, ciliary dyskinesia).
- Older patients, particularly well-vaccinated dogs without exposure to organisms associated with canine infectious respiratory disease complex (CIRDC), often have underlying disease.

#### Causes

- Primary respiratory tract pathogens include *Bordetella bronchiseptica* and *Streptococcus equi* subsp *zooepidemicus* in dogs and cats and *Mycoplasma cynos* in dogs.
  - Other *Mycoplasma* spp may be primary pathogens in dogs and cats.
- *B bronchiseptica* has been isolated from tracheal wash fluid in 50%-70% of puppies with community-acquired pneumonia.<sup>1,2</sup>

CIRDC = canine infectious respiratory disease complex



continues

## Underlying Conditions & Predisposing Factors

### Primary Bacterial Pneumonia

- Exposure to infected animals
- Decreased immunity
  - Immature immune system
  - Immune compromise
    - Immune system disease
    - Immunosuppressive therapy
    - Systemic disease
- Lack of vaccination
- Environmental stress

### Secondary Bacterial Pneumonia Airway Origin

- Compromised local defenses
- Viral or bacterial infection
  - *B bronchiseptica*
  - Distemper
  - Influenza

- Canine parainfluenza virus
- Other respiratory viruses or some *Mycoplasma* spp
- Chronic bronchitis in dogs or cats (eg, feline asthma)
- Ciliary dyskinesia
- Inhalation damage (smoke, gastric acid)
- Aspiration
  - Esophageal disease
    - Megaesophagus
    - Esophagitis
    - Foreign body
    - Stricture, obstruction
    - Esophageal dysmotility
  - Oropharyngeal disease
    - Laryngeal paralysis
      - Postsurgery
      - Associated esophageal dysmotility

- Brachycephalic airway syndrome
- Cleft palate
- Cricopharyngeal motor dysfunction
- Neuromuscular disorders
  - Myasthenia gravis
  - Polyneuropathy
  - Polymyopathy
  - Decreased mentation
- Iatrogenic associations
  - Anesthesia
  - Sedation
  - Force feeding
  - Feeding tube misplacement

### Hematogenous

- Infection in other organs
- Wounds

- Opportunistic infections are typically caused by organisms residing in the oropharynx or nasopharynx.
- Organisms associated with CIRDC can cause primary bacterial pneumonia or can predispose the animal to opportunistic infections.
  - A recent study found canine parainfluenza virus in 7 of 20 dogs diagnosed with bacterial pneumonia involving organisms other than *B bronchiseptica*.<sup>3</sup>

### Risk Factors

- Primary respiratory infections are acquired from exposure to other infected animals or fomites.
  - Exposure could occur in locations such as shelters or rescue housing, pet stores, breeding operations,

boarding or grooming facilities, and dog parks.

- Exposure to animals (or the toys or bowls of animals) with unknown vaccination history or incomplete vaccinations against respiratory pathogens increases potential for infection.
- Animals with immature or compromised immune systems and those that have not been vaccinated against respiratory pathogens are at increased risk if exposed to infected animals or materials.
- Numerous underlying conditions or predisposing factors lead to bacterial pneumonia from opportunistic organisms (see **Underlying Conditions & Predisposing Factors**).

### Pathophysiology

- Bacteria typically enter the lungs through the airways, either through inhalation of primary infectious agents or aspiration of oral, pharyngeal, esophageal, or gastric contents.
- Hematologic seeding of the lung with bacteria from elsewhere in the body can also occur.
  - This route of infection is likely underdiagnosed because thoracic radiographs typically show a diffuse interstitial to alveolar pattern rather than the more classic gravity-dependent alveolar pattern of bronchogenic or aspiration pneumonia.
  - A hematogenous origin was documented in more than half of cats with bacterial pneumonia based on necropsy.<sup>4</sup>



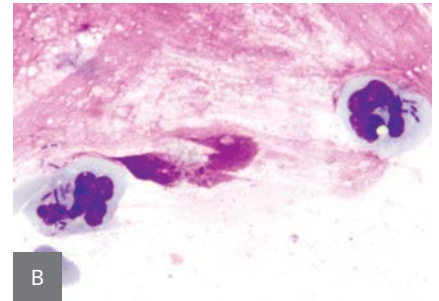
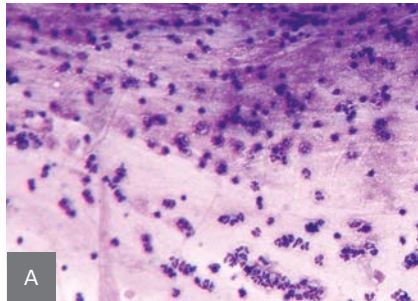
- Clinical signs result from damage to the airway epithelium, influx of inflammatory cells, edema, and mucus hypersecretion.

### History

- Signs are most often acute (ie, of only a few days' duration) but can be present for several months.
- Cough is a common sign.
- Signs of compromised lung function include (in order of increasing severity): increased resting respiratory rate, increased respiratory effort during mild activity, respiratory distress, and cyanosis.
- Systemic inflammatory signs (eg, lethargy, inappetance) may be present.
- Careful questioning is indicated to identify risk factors, predisposing conditions (eg, anesthesia), and exposure to primary pathogens.

### Physical Examination

- Auscultation of crackles, loudest in the cranioventral lung lobes, is the classic finding.
  - Auscultation must include positioning the stethoscope in the axilla, under which the cranial lung lobes are positioned.
  - Although crackles in any lobe in a previously healthy animal is an important finding, absence of crackles does not eliminate possibility of pneumonia.
    - Crackles were reported in only 9% to 25% of dogs with aspiration pneumonia.<sup>5,6</sup>
- Increased respiratory effort, orthopnea, respiratory distress, or cyanosis is present with sufficient compromise.
- Signs of systemic inflammation, such as fever and depression, *may* be present.
  - Fever is present in only about



**1** Tracheal wash fluid from a dog with septic inflammation. At low magnification (A), neutrophils and mucus are abundant. At high magnification (B), intracellular and extracellular rod-shaped bacteria can be seen. (Modified Wright's stain)

one-third of dogs with aspiration pneumonia<sup>5,6</sup> and is considered uncommon in cats with lower respiratory tract infections.<sup>7</sup>

- A normal temperature *does not* rule out bacterial pneumonia.

## **Dx** Diagnosis

### Definitive Diagnosis

- Confirmation of diagnosis requires cytologic demonstration of septic inflammation in an airway specimen—usually a tracheal wash (**Figure 1**).
- A positive bacterial culture confirms the involvement of specific organism(s) and provides valuable information for guiding antibiotic selection.
  - Previously healthy patients with mild-to-moderate disease and no risk factors for antibiotic-resistant infection may not require airway sampling and are usually treated empirically based on other clinical information.
  - Severely compromised animals may be too unstable to tolerate collection of an airway specimen and are likewise treated empirically without delay.
  - Tracheal wash is most likely to

provide a representative specimen in pneumonia of airway origin.

- Bronchoalveolar lavage (BAL) may be indicated if radiographs suggest interstitial disease, as this is more likely than tracheal wash to provide a representative specimen in such cases.
- If possible, tracheal wash (or BAL) should be performed before antibiotic administration.
- After antibiotic administration, cytology and culture are often falsely negative for infection.\*
- Infection with multiple species of organisms is common.
- *Mycoplasma* spp infections are difficult to diagnose because organisms are not apparent cytologically, and a specific culture must be requested.
  - Polymerase chain reaction (PCR) testing is available and is considered more sensitive than culture.
  - The role of *Mycoplasma* spp as a primary pathogen is unknown, so coinfections should be considered.
  - The value of *Mycoplasma* spp testing in individual cases is debatable, but the author recommends testing in dogs with

BAL = bronchoalveolar lavage, CIRDC = canine infectious respiratory disease complex, PCR = polymerase chain reaction  
\*Based on anecdotal clinical experience.

continues

suspected exposure to CIRDC organisms and in cats.

- A presumptive diagnosis of pneumonia is made with suggestive history, physical examination, CBC, and/or thoracic radiographic findings.

### Differential Diagnosis

- The main differential diagnosis for patients with airway origin pneumonia is sterile aspiration pneumonia.
  - In dogs and cats, however, bacterial infection is common following aspiration.
- An important differential is congestive heart failure.
  - Cats with congestive heart failure can have patchy, asymmetric alveolar infiltrates on thoracic radiographs that mimic those of bacterial pneumonia.
  - Attention should be paid to the size of the heart and pulmonary veins.
  - Echocardiography and ProBNP can be useful.
- Diagnostic differentials for hematogenous pneumonias are many and include infection with other organisms (eg, viruses, protozoa, fungi), interstitial lung disease (including eosinophilic bronchopneumopathy), neoplasia, hemorrhage, and pulmonary edema (among others).
- Dogs with typical CIRDC have self-limiting tracheobronchitis.
  - Bacterial pneumonia can occur as a result of bacteria associated with CIRDC or secondary to viral infections of CIRDC.
- Cats with bacterial pneumonia can present with signs consistent with feline asthma.

### Laboratory Findings

- Neutrophilic leukocytosis with left shift supports a diagnosis of bacterial pneumonia.

- Only 40% to 60% of dogs with aspiration pneumonia have increased numbers of bands<sup>5,6</sup>; therefore, bacterial pneumonia *cannot* be ruled out on the basis of a normal CBC.

### Imaging

- Airway-origin pneumonia most often results in a bronchoalveolar pattern, most severe in one or more of the gravity-dependent lung lobes (right or left cranial and right middle lobes).
- Hematogenous origin pneumonia most often results in a diffuse interstitial or mixed pattern, which may be most severe in the caudal–dorsal lung lobes.
- Bacterial infection associated with a foreign body may result in a localized interstitial, alveolar, or consolidated pattern.
- Thoracic radiographs should be scrutinized for signs of concurrent or predisposing disease within the lung or in other organs, particularly megaesophagus, bronchiectasis, lung lobe torsion, or cavitory disease.

### Other Diagnostics

- Ultrasound can be performed in areas of lung consolidation if neoplasia, foreign body, abscess, or lung lobe torsion are differentials.
- Computed tomography is often pursued in patients with recurrent or nonresponsive pneumonia to search for underlying or complicating disease (eg, foreign bodies, bronchiectasis, neoplasia, abscess).
- Bronchoscopy is likewise often conducted in patients with recurrent or nonresponsive pneumonia.
  - Bronchoscopy is performed if airway specimens are needed but tracheal wash is unrewarding or radiographic location of disease (eg, primarily interstitial) makes

a successful tracheal wash less likely.

### Postmortem Findings

- If death occurs before antibiotic administration, septic inflammation with isolation of organisms from tissue culture or PCR is expected.
- Characteristic findings may be obscured by prior treatment.
- In the absence of a known cause for pneumonia prior to death, virus isolation or PCR should be considered and all other organs carefully investigated.

## Treatment

### Inpatient or Outpatient

- Hospitalization is required for oxygen administration in distressed patients, for fluid administration in dehydrated patients, and for IV antibiotic treatment for patients with systemic inflammatory response syndrome or with esophageal or GI disease that would interfere with the absorption of oral medications.
- Stable, hydrated patients can be treated as outpatients.
- Patients with suspected or confirmed infection with organisms associated with CIRDC or with multidrug-resistant bacteria should be managed using isolation protocols.

### Medical

- Antibiotic administration and maintenance of systemic hydration are indicated for all patients.
- Nebulization of sterile saline may improve mucociliary clearance in patients with severe clinical signs and lung consolidation.
  - Antibiotics can be administered by nebulization, but this route is reserved for resistant organisms to avoid systemic toxicity of parenteral drugs and is considered inadequate

as the sole antibiotic coverage for patients with pneumonia.

- Bronchoconstriction may be induced by nebulization with medication other than sterile saline.
- Systemic antibiotics are the primary treatment for bacterial pneumonia.
- Coupage may also help to promote airway clearance and can be performed for 5-10 minutes several times daily.
  - Coupage is indicated following nebulization.
  - Encouraging activity and frequent turning of recumbent patients is likely more effective, however, and coupage should not replace these treatments.

#### Nutritional Aspects

- Attention to nutrition is indicated for all patients with infection, particularly if systemic signs are present.
- Gastric tubes or parenteral nutrition may be considered for patients with esophageal or GI disease.

#### Activity

- Clearance of exudate from the lung is enhanced by exercise as a result of changes in body position, increased tidal volumes, and stimulation of productive cough.
  - Patients should be encouraged to exercise to the extent their respiratory function allows.
- Patients that are unable to stand should be rotated from side to side and to sternal recumbency every 2 to 4 hours.

#### Client Education

- Specific discussion points will depend on disease severity, the origin of the bacterial pneumonia, and underlying or predisposing problems.
- Pneumonia secondary to CIRDC

**Table. Antibiotics for Bacterial Pneumonia**

Drug	Species	Dose
Amoxicillin	Dogs, cats	22 mg/kg PO q8h
Ampicillin with sulbactam	Dogs, cats	22 mg/kg IV q8h (ampicillin)
Amoxicillin with clavulanate	Dogs	15–25 mg/kg PO q8h
	Cats	10–20 mg/kg PO q8h
Cephalexin	Dogs, cats	20–40 mg/kg PO q12h
Clindamycin	Dogs, cats	5.5–11 mg/kg PO, IV, or SC q12h
Doxycycline	Dogs, cats	5–10 mg/kg PO or IV q12h
Enrofloxacin	Dogs	5–10 mg/kg PO, IV, or SC q24h
Marbofloxacin	Dogs, cats	2.7–5.5 mg/kg PO q24h
Trimethoprim–sulfonamide	Dogs, cats	15 mg/kg PO q12h

warrants a discussion of the benefits and limitations of routine vaccination as well as isolation of the patient to avoid spread of disease.

#### Alternative Therapy

- Shorter courses of antibiotics are used in humans with community-acquired pneumonia, which may be analogous to dogs that have bacterial pneumonia as a complication of CIRDC.
  - In the author's experience, short courses of antibiotics in dogs or cats with chronic or recurrent disease, or with underlying or predisposing factors, are not likely to be successful.

## Medications

#### Drugs and Fluids

- Ideally, antibiotic selection is based on results of bacterial culture and susceptibility testing (**Table**).
- Pending culture results, or if testing was not performed, some general

guidelines follow.

- Monitoring for response to treatment is indicated regardless of how antibiotics are selected, with a positive response expected within 72 hours.
- For patients with mild or moderate disease, consider amoxicillin with clavulanate, cephalexin, or trimethoprim–sulfonamide.
- If pneumonia is suspected to be associated with CIRDC, consider doxycycline for its historic activity against many *Bordetella* spp isolates and efficacy against *Mycoplasma* spp.
  - This drug has a narrow spectrum for gram-negative organisms and should not be used as the sole drug for patients with moderate-to-severe signs.
- For patients with severe or life-threatening disease, broader-spectrum antibiotic coverage may be prudent and might include ampicillin/sulbactam and a fluoroquinolone, ampicillin/sulbactam and an aminoglycoside, or clinda-

continues

mycin and a fluoroquinolone.

- It is generally recommended that antibiotics be continued for 1-2 weeks beyond the resolution of clinical and radiographic signs of disease.
  - Treatment for 4-6 weeks is typical.
  - Shorter courses may be sufficient in acute cases with no ongoing underlying or predisposing conditions, such as those with pneumonia associated with CIRDC.
- Careful attention to hydration status, with administration of IV fluids as needed, is essential to maximize mucociliary clearance and support local circulation.
  - Over-hydration may contribute to pulmonary edema.
- Bronchodilators (theophyllines or  $\beta$ -agonists) may be indicated in cats with associated bronchoconstriction.
  - They might be helpful in distressed dogs through potential mechanisms such as improved mucociliary clearance or anti-inflammatory effects, but they can potentially worsen ventilation-perfusion mismatch and should be used cautiously.
- Corticosteroids at anti-inflammatory doses may be indicated in life-threatening situations.
  - Whether they are ultimately beneficial or harmful remains undetermined.

**Contraindications**

- Diuretics, such as furosemide, contribute to dehydration of airway secretions and should be avoided.
- Cough suppressants are generally not indicated and could interfere with coughing's beneficial effects.
  - Dogs with severe cough, such as that resulting from concurrent

or underlying tracheal collapse, chronic bronchitis, or CIRDC, may benefit from judicious suppression to minimize fatigue and break a cycle of cough followed by inflammation.

**Precautions & Drug Interactions**

- Fluoroquinolones can delay the clearance of theophylline; if both are chosen, the dosing interval of theophylline should be increased 2-fold.

 **Follow-up**

**Patient Monitoring**

- Patient monitoring is critical.
- Selected antibiotics may not be sufficient to treat all organisms involved, and unidentified or untreatable underlying conditions may delay recovery or result in re-infection.
  - A positive response to antibiotics is expected within 72 hours of initiating treatment.
- Patients with moderate-to-severe disease requiring hospitalization are monitored by careful physical examination at least twice daily.
  - Thoracic radiographs and CBC are performed every 48-72 hours in most cases.
  - Additional monitoring may be indicated depending on predisposing, concurrent, or complicating conditions.
  - Following discharge, patients are evaluated every 1-2 weeks until signs have resolved.
    - Depending on abnormalities detected initially, monitoring typically includes CBC and thoracic radiography along with a complete physical examination.
- It may be sufficient in patients with mild disease to follow up with periodic phone calls and a single office visit to allow for a complete physical

examination.

- Patients with persistent or recurrent signs may require more aggressive follow-up with airway specimen collection or more advanced diagnostic testing, such as CT or bronchoscopy.

**Complications**

- Acute complications include sepsis, respiratory failure, and death.
- Chronic complications are rare but include lung abscess formation.
- Failure to respond to treatment or recurrence suggests either an ongoing underlying or predisposing problem and/or infection with a resistant organism.

 **In General**

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**Cost Key**  
 \$ = up to \$100  
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 \$\$\$ = \$251–\$500  
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- Bacterial pneumonia in otherwise healthy individuals resulting from a single event, such as aspiration following anesthesia or as a complication of CIRDC, may resolve readily and completely with a course of antibiotic therapy on an outpatient basis.
- Patients with severe disease may require intensive care for 1 week or longer.
- Patients with underlying problems that cannot be corrected are candidates for recurrent episodes.
- A study of dogs with aspiration pneumonia reported a median hospitalization of 3 days (range, 0-11 days) at a mean cost of \$2581 (range, \$241-\$10400).<sup>5</sup>

CIRDC = canine infectious respiratory disease complex

### Prognosis

- Short-term prognosis can be good to grave.
- Long-term prognosis depends on the origin of infection and underlying or predisposing factors.
- Two studies of dogs with aspiration pneumonia reported 72% and 77% survival, respectively.<sup>5,8</sup>

### Prevention

- Risk for contracting primary bacterial pneumonia or pneumonia as a complication of CIRDC can be minimized by avoiding contact with susceptible populations and by routine vaccination, as indicated by individual patient circumstance.
- Careful attention to technique can minimize risk for aspiration from iatrogenic causes.

- Aggressively seeking and managing predisposing factors is indicated in patients with unexplained disease.

■ cb

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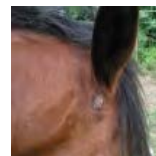
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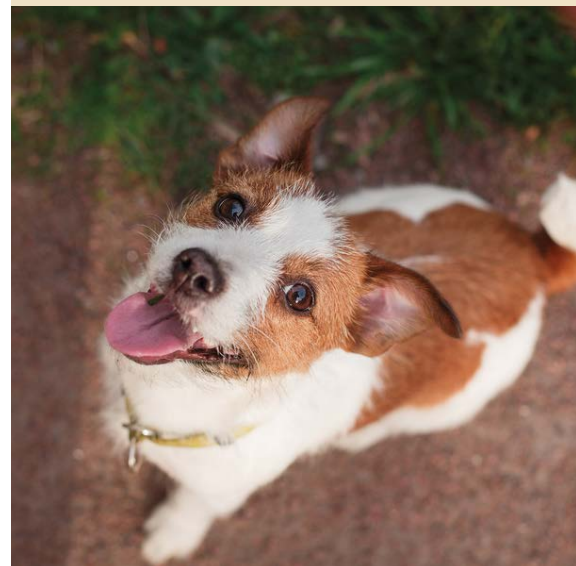
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### The Millionth Urolith

The **Minnesota Urolith Center (MUC, urolithcenter.org)**, which seeks to reduce incidence of urinary disease in companion animals and enhance veterinary and nutritional care of pets with urinary tract disorders, recently celebrated the analysis of its millionth urolith. With support from long-term partner **Hill's Pet Nutrition (HillsVet.com)**, the MUC delivers an analysis service to veterinarians globally and enables them to access results and other information easily. Part of the University of Minnesota College of Veterinary Medicine, the MUC analyzes and treats urinary stones. It also researches risk factors for urolithiasis and science-supported recommendations for urolith prevention.—*Press release 6/2015*

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**Vetnique Labs (glandex.com)**

recently introduced a soft-chew version of its popular veterinary supplement Glandex. **Glandex Soft Chews**, which come as an easy-to-use once-daily treat, help support healthy anal gland function in dogs. They contain the same active ingredients as the original Glandex but in a peanut butter soft chew.—*Press release 6/2015*



### Treating Chemotherapy-Induced Diarrhea

**Jaguar Animal Health (jaguaranimalhealth.com)** recently announced that it had completed a multi-site pilot safety study involving the anticipated commercial formulation of **Canalevia**—a canine-specific formulation of crofelemer, an anti-secretory active pharmaceutical ingredient isolated and purified from the *Croton lechleri* tree—in dogs suffering from chemotherapy-induced diarrhea (CID). Pending approval from the USFDA, the company expects to launch Canalevia for CID in dogs by early 2016.—*Press release 7/2015*

### Pro-Pectalin Powder

**Vétoquinol (vetoquinolusa.com)** last month announced the launch of a new form of their popular **Pro-Pectalin** product line, now available to veterinarians in a water-soluble powder as well as the previously available tablets and dial-a-dose gels. Pro-Pectalin products contain kaolin, pectin, and *Enterococcus faecium* to help soothe irritated intestines and restore normal intestinal bacteria balance.—*Press release 7/2015*

### Raising Their Voyces

During the AVMA Convention 2015, **i4C Innovations** launched the **Voyce Pro (voycepro.com)**, which enables remote supervision of canine patients' vital signs and wellness indicators (eg, heart and respiratory rates, intensity of activity, calories burned, distance traveled, quality of rest). Worn around patients' necks, Voyce Health Monitors can be set to customized data parameters for each patient; the veterinarian is notified if the vital signs and wellness indicators move outside of those parameters.—*Press release 7/2015*

### An Antibody Experience

Independent antibody search engine **CiteAb (citeab.com)** has released a new dataset ([bit.ly/1SdqNkG](http://bit.ly/1SdqNkG)) that highlights leading research institutions and antibody suppliers in the veterinary research market. It also outlines the countries seeing growth in the field. CiteAb amasses its data from analysis of hundreds of thousands of life sciences publications that use research antibodies. Although veterinary research makes up a small percentage (0.5%) of the antibody market, CiteAb's data shows that the sector is growing. In terms of veterinary antibody use, the US leads markets with 20.66% of the total. There has been a significant increase in veterinary antibody use in China, now in the global top 5 and continuing to grow rapidly. New Zealand, Belgium, and Brazil also feature high in veterinary antibody use.—*Press release 7/2015*

### Label Update for Cerenia

**Zoetis** recently announced that the USFDA approved an update to labeling for **Cerenia (zoetis.com/products/pages/cerenia/extended-therapy.aspx)** tablets.

The revised label allows for once-daily administration until resolution of acute vomiting for dogs 7 months of age and older. Previously, the dosing and administration instructions limited use to 5 consecutive days, which remains the dosing limitation for dogs 2 to 7 months of age. Cerenia (maropitant citrate), indicated for prevention of acute vomiting in dogs and the prevention of vomiting caused by motion sickness in dogs, is also available as an injectable formulation.—*Press release 6/2015*



continues

**In the Loop**

**Assisi Animal Health** ([assisianimalhealth.com](http://assisianimalhealth.com)) unveiled the **Assisi Loop 2.0**, a non-pharmaceutical antiinflammatory device, at AVMA last month. The Assisi Loop uses patented targeted pulsed electromagnetic field (tPEMF) technology that has been demonstrated to affect known biochemical and cellular mechanisms related to inflammation, with results published in peer-reviewed journals. The Assisi Loop, available only through veterinary professionals, is prescribed by veterinarians to treat orthopedic injuries, degenerative neurological issues, post-surgical pain and swelling, inflammatory conditions, and wounds. The USFDA has approved the technology for treating post-operative pain and edema in humans. Although not required for veterinary medical devices, Assisi is funding clinical trials for this innovation in pain management for veterinary medicine.—  
*Press release 7/2015*

**Nestlé's on the Job**

Nestlé in the United States and **Nestlé Purina PetCare Company** have launched **Project Opportunity**, a new career-acceleration initiative to help people gain work experience and strengthen their professional development skills. Project Opportunity, part of Nestlé's broader efforts to develop talent for the company and help tackle the global unemployment crisis, will include increasing the number of trainees, interns, and apprentices at Nestlé ([nestlepurinacareers.com](http://nestlepurinacareers.com)).—  
*Press release 7/2015*

**Smart Collar Case Study**

PetPace ([petpace.com](http://petpace.com)), the provider of a smart collar for monitoring pets' vital signs, recently released findings from a new case study, which documents how a smart collar provided crucial posture monitoring to alleviate breathing difficulties for a 4-year-old Chihuahua that had been hit by a car. Following the accident, the patient was hospitalized for treatment and close observation. It was breathing heavily, which raised clinical suspicion of an internal chest injury, and was placed on its stomach; if allowed to lie on its side, the dog became distressed and its breathing labored. To prevent the patient's breathing from deteriorating if it rolled on its side, a PetPace smart collar was used. It provided minute-by-minute readings of the dog's posture and automatically alerted hospital staff when it rolled so that caretakers could immediately move the dog to alleviate its labored breathing.—  
*Press release 7/2015*

**Flea-Free in Florida**

**Merial** recently released results from a **NexGard** ([nexgardfordogs.com](http://nexgardfordogs.com)) study, published by **Parasites & Vectors** ([bit.ly/1K439oX](http://bit.ly/1K439oX)), conducted with privately owned dogs in Tampa in summer 2014. Flea-infested dogs were treated with 2 monthly doses of **NexGard** (afoxolaner) chewables. Flea counts on dogs were reduced more than 99% 7 days after the first treatment, and 97% of dogs evaluated were flea-free 2 weeks after the initial treatment. There were no fleas on any dog when evaluated 2 weeks after the second treatment was administered (6 weeks after the initial treatment).—  
*Press release 7/2015* ■ **cb**



**Caution**

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

**Indications**

SENTINEL SPECTRUM® (milbemycin oxime/lufenuron/praziquantel) is indicated for the prevention of heartworm disease caused by *Dirofilaria immitis*; for the prevention and control of flea populations (*Ctenocephalides felis*); and for the treatment and control of adult roundworm (*Toxocara canis*, *Toxascaris leonina*), adult hookworm (*Ancylostoma caninum*), adult whipworm (*Trichuris vulpis*), and adult tapeworm (*Taenia pisiformis*, *Echinococcus multilocularis* and *Echinococcus granulosus*) infections in dogs and puppies two pounds of body weight or greater and six weeks of age and older.

**Dosage and Administration**

SENTINEL SPECTRUM should be administered orally, once every month, at the minimum dosage of 0.23 mg/lb (0.5 mg/kg) milbemycin oxime, 4.55 mg/lb (10 mg/kg) lufenuron, and 2.28 mg/lb (5 mg/kg) praziquantel. For heartworm prevention, give once monthly for at least 6 months after exposure to mosquitoes.

**Dosage Schedule**

Body Weight	Milbemycin Oxime per chewable	Lufenuron per chewable	Praziquantel per chewable	Number of chewables
2 to 8 lbs.	2.3 mg	46 mg	22.8 mg	One
8.1 to 25 lbs.	5.75 mg	115 mg	57 mg	One
25.1 to 50 lbs.	11.5 mg	230 mg	114 mg	One
50.1 to 100 lbs.	23.0 mg	460 mg	228 mg	One
Over 100 lbs.	Administer the appropriate combination of chewables			

To ensure adequate absorption, always administer SENTINEL SPECTRUM to dogs immediately after or in conjunction with a normal meal.

SENTINEL SPECTRUM may be offered to the dog by hand or added to a small amount of dog food. The chewables 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 a few minutes after administration to ensure that no part of the dose is lost or rejected. If it is suspected that any of the dose has been lost, redosing is recommended.

**Contraindications**

There are no known contraindications to the use of SENTINEL SPECTRUM.

**Warnings**

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

**Precautions**

Treatment with fewer than 6 monthly doses after the last exposure to mosquitoes may not provide complete heartworm prevention.

Prior to administration of SENTINEL SPECTRUM, dogs should be tested for existing heartworm infections. At the discretion of the veterinarian, infected dogs should be treated to remove adult heartworms. SENTINEL SPECTRUM is not effective against adult *D. immitis*.

Mild, transient hypersensitivity reactions, such as labored breathing, vomiting, hypersalivation, and lethargy, have been noted in some dogs treated with milbemycin oxime carrying a high number of circulating microfilariae. These reactions are presumably caused by release of protein from dead or dying microfilariae.

Do not use in puppies less than six weeks of age.

Do not use in dogs or puppies less than two pounds of body weight.

The safety of SENTINEL SPECTRUM has not been evaluated in dogs used for breeding or in lactating females. Studies have been performed with milbemycin oxime and lufenuron alone.

**Adverse Reactions**

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

To report suspected adverse drug events, contact Virbac at 1-800-338-3659 or the FDA at 1-888-FDA-VETS.

**Information for Owner or Person Treating Animal**

*Echinococcus multilocularis* and *Echinococcus granulosus* are tapeworms found in wild canids and domestic dogs. *E. multilocularis* and *E. granulosus* can infect humans and cause serious disease (alveolar hydatid disease and hydatid disease, respectively). Owners of dogs living in areas where *E. multilocularis* or *E. granulosus* are endemic should be instructed on how to minimize their risk of exposure to these parasites, as well as their dog's risk of exposure. Although SENTINEL SPECTRUM was 100% effective in laboratory studies in dogs against *E. multilocularis* and *E. granulosus*, no studies have been conducted to show that the use of this product will decrease the incidence of alveolar hydatid disease or hydatid disease in humans. Because the prepatent period for *E. multilocularis* may be as short as 26 days, dogs treated at the labeled monthly intervals may become reinfected and shed eggs between treatments.

Manufactured for: Virbac AH, Inc.  
P.O. Box 162059, Ft. Worth, TX 76161

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Dogs should be tested for heartworm prior to use. Mild hypersensitivity reactions have been noted in some dogs carrying a high number of circulating microfilariae. Treatment with fewer than 6 monthly doses after the last exposure to mosquitoes may not provide complete heartworm prevention. Please see full product label for more information, or visit [www.virbacvet.com](http://www.virbacvet.com).

See page 78 for product information summary.

**References:** 1. Trifexis<sup>®</sup> [product label]. Indianapolis, IN: Elanco; 2014.  
2. Heartgard<sup>®</sup> Plus [product label]. Duluth, GA: Merial Inc; 2011.

\* *A. caninum*.

† Prevents flea eggs from hatching; is not an adulticide.

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# European Veterinary Conference Voorjaarsdagen ■ 9–11 April 2015 ■ Amsterdam

The annual European Veterinary Conference Voorjaarsdagen (translated, means *spring days*) is held in Amsterdam, The Netherlands, where more than 1000 veterinarians and hundreds of veterinary technicians gather for 3 days of practical lectures and sessions.

## Small Intestinal Dysbiosis

Small intestinal dysbiosis refers to alterations in small intestinal microbiota numbers and/or composition. Antibiotic-responsive diarrhea, tylosin-responsive diarrhea, intestinal dysbiosis, and small intestinal bacterial overgrowth are terms describing similar conditions; it is unknown, however, whether they describe the same clinical entity, as the underlying cause of these conditions can be difficult to elucidate. Existing protective mechanisms that help prevent dysbiosis include gastric acid, intestinal motility (especially the propulsive small intestinal movements), and antibacterial activity of pancreatic juice. Disease affecting any of these mechanisms could lead to small intestinal dysbiosis. The diarrhea associated with small intestinal dysbiosis is chronic and may be intermittent. Weight loss is variably present. Duodenal juice cultures are difficult to perform and/or interpret. The most practical, albeit insensitive, diagnostic test is the combination of serum folate and cobalamin concentrations. Serum Trypsin-like immunoreactivity should also be measured, as enzymatic treatment of exocrine pancreatic insufficiency patients will generally negate the need for further therapies. Treatments for patients without an identifiable primary cause include antibiotics (eg, tylosin 25 mg/kg q12h for 6 weeks), prebiotics (eg, fructooligosaccharides), probiotics, and synbiotics (ie, a combination of pre- and probiotics). Likely the most practical synbiotic approach is to use a prebiotic-fortified food with additional probiotic supplementation. Cobalamin supplementation may be beneficial for some. Some patients require prolonged or life-long antimicrobial therapy.—*Steiner J*

## Respiratory Disease in Pet Rodents

Respiratory disease is commonly seen in rodents, which are increasingly popular as pets. Poor husbandry and diet are often implicated as underlying causes of respiratory illness in pet rodents. A large, properly ventilated cage is essential to help prevent ammonia buildup, which can act as a potent respiratory irritant, potentiating opportunistic respiratory colonization. In addition, it is recommended to avoid overcrowding and not to house different species together, as some animals may be carriers of organisms that are pathogenic to a different species. Weight loss, anorexia, poor coat condition, red ocular or nasal staining, sneezing, dyspnea, wheezing, and nasal discharge can all be signs of respiratory disease in rodents. Care must be taken to not stress a dyspneic rodent during physical examination.

Diagnostics to consider include thoracic radiographs and culture and susceptibility testing of nasal swabs or tracheal/bronchial lavage fluid. Numerous viruses and bacteria—including *Mycoplasma pulmonis*, Sendai virus, *Bordetella bronchiseptica*, *Streptococcus pneumoniae*, and rat coronaviruses—cause respiratory illness in rodents. Less

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common causes of respiratory disease, such as pulmonary/alveolar histiocytosis, foreign body pneumonitis, and metastatic disease should be considered as well.

Treatment is aimed at controlling the organism and improving quality of life. Therapies may include oxygen, systemic and nebulized antimicrobials, and nutritional support. Corticosteroids are considered in end-stage disease. Owners must understand that relapses after initial clinical response are common.  
—Mancinelli E

### Gastritis and Gastric Ulcers

Gastric disease in dogs and cats can be secondary to clinical conditions including gastric ulceration, gastritis, neoplasia, or inflammatory infiltration of the gastrointestinal tract. Gastritis, or gastric mucosal inflammation, may be acute, chronic, idiopathic, or secondary to underlying causes. *Physaloptera rara*, the stomach worm, although rare and difficult to diagnose, should be considered in patients with chronic vomiting. Combination antibiotic usage along with an antacid is often successful in treating *Helicobacter* spp-like organisms when identified in patients with chronic gastritis unresponsive to traditional therapy. Gastric ulcerations or erosions are areas of

damaged gastric mucosa that can cause more severe issues including significant blood loss and life-threatening gastrointestinal perforations. Therapy is aimed at treating or removing the underlying cause, most commonly ulcerogenic drugs (eg, NSAIDs) or corticosteroids, which diminish the natural protective mechanisms of the stomach lining. Medications used to treat gastric ulcers include agents such as calcium carbonate or aluminum hydroxide, which buffer gastric acid in the gastric lumen. Additionally, antacids such as H<sub>2</sub>-receptor antagonists (eg, famotidine) and proton pump inhibitors (eg, omeprazole) may be effective at decreasing gastric acid secretion. Sucralfate is a gastromucosal protectant that relies on gastric acid exposure to break down into its active ingredient; this adheres to damaged gastric tissue. Misoprostol, a synthetic prostaglandin, is highly effective at preventing ulceration in patients receiving NSAIDs or glucocorticoids, but utility for treatment of existing lesions is unproven.—Steiner J

### Feline Hereditary Diseases—Peculiarities and Recent Progress

More than 230 hereditary disorders and genetic predispositions, similar to those in dogs, are known; molecular genetic tests are available for more than 2 dozen. Some of these

continues

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disorders represent possible models for studying similar diseases in humans. Feline breed variability is more restricted than canine breed variability, with several simple attributes (dominant or recessive) distinguishing the breeds. Single nucleotide polymorphism panels can define breeds and disease-causing mutations; most are autosomal recessive traits, whereas others are X-chromosomal recessive or autosomal dominant with incomplete penetrance. These disorders span hematologic problems, muscular diseases, storage diseases, heart defects, metabolic derangements, renal disorders, and ocular diseases; DNA testing is available for many of these. Though hereditary eye disorders are uncommon in cats, 2 retinopathies are seen in Abyssinians. Hereditary bleeding disorders are also rare, but coagulation factor XII deficiency is seen in many DSH cats. In some breeds, hip dysplasia and patellar luxation are more common than previously thought. Cancer is less attributable to genetics in cats than in dogs, except in the case of lymphoma. Some cats also appear to have a genetic predisposition for certain viral infections. Cats are more amenable to transplantation, and immune-mediated diseases are less common. The feline genome sequence has been recently completed, which will greatly enhance the understanding of feline hereditary disease.—*Giger U*

## Esophageal Problems in Dogs and Cats

The normal esophagus is lined by squamous epithelium and bicarbonate-rich mucus. The musculature is composed entirely of striated muscle in dogs, whereas in cats the bottom 30%-50% is smooth muscle. Regurgitation may be the only clinical sign of esophageal pathology and must be distinguished from vomiting and dysphagia. Clinical examination and observation of the patient eating food from the floor vs an elevated point may help differentiate between the 2. Pharyngeal or throat paralysis, enlarged lymph nodes, non-compressible thorax (in small dogs and cats) or neurologic signs commonly accompany an esophageal problem. Myasthenia gravis or megaesophagus secondary to endocrinopathies should be ruled out. Radiology is an excellent diagnostic tool, with fluoroscopy, radiocontrast swallows (iodine preferred over barium), and endoscopy providing ancillary help. Foreign bodies are a common esophageal problem. Esophagitis may occur secondary to a host of insults to the esophageal lining. Fasting, fluid therapy, H<sub>2</sub> blockers, and sucralfate treat the mucosal damage caused by such events. Prokinetics and a gastric tube may also be necessary. Esophageal strictures have similar causes and treatment includes balloon dilatation or bougienage. Judicious use of corticosteroids may be used to decrease inflammation and

## Carprieve® (carprofen) Injection

Non-steroidal anti-inflammatory drug. For subcutaneous use in dogs only.

**BRIEF SUMMARY:** Before using, consult the product insert, a summary of which follows.

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

**INDICATIONS:** For relief of pain and inflammation associated with osteoarthritis and for control of postoperative pain associated with soft tissue and orthopedic surgeries in dogs.

**CONTRAINDICATIONS:** Carprofen should not be used in dogs exhibiting previous hypersensitivity to carprofen.

**WARNINGS:** Keep out of reach of children. Not for human use. Consult a physician in cases of accidental human exposure. **For use in dogs only.** Do not use in cats. All dogs should undergo a thorough history and physical examination before initiation of NSAID therapy. Appropriate laboratory tests to establish hematological and serum biochemical baseline data prior to, and periodically during, administration of any NSAID should be considered. **Owners should be advised to observe for signs of potential drug toxicity (see Adverse Reactions, Animal Safety and Post-Approval Experience).**

**PRECAUTIONS:** As a class, cyclooxygenase inhibitory NSAIDs may be associated with gastrointestinal, renal and hepatic toxicity. The use of parenteral fluids during surgery should be considered to reduce the potential risk of renal complications when using NSAIDs perioperatively. The most frequently reported effects have been gastrointestinal signs. Events involving suspected renal, hematologic, neurologic, dermatologic, and hepatic effects have also been reported. Patients at greatest risk for renal toxicity are those that are dehydrated, on concomitant diuretic therapy, or those with renal, cardiovascular, and/or hepatic dysfunction. Concurrent administration of potentially nephrotoxic drugs should be approached cautiously, with appropriate monitoring. Concomitant use of carprofen with other anti-inflammatory drugs, such as other NSAIDs or corticosteroids, should be avoided because of the potential increase of adverse reactions, including gastrointestinal ulcerations and/or perforations. Carprive Injection is not recommended for use in dogs with bleeding disorders (e.g., Von Willebrand's disease), as safety has not been established in dogs with these disorders. The safe use of Carprive Injection in animals less than 6 weeks of age, pregnant dogs, dogs used for breeding purposes, or in lactating bitches has not been established. Safety has not been established for IV or IM administration. If additional pain medication is warranted after administration of the total daily dose of carprofen, alternative analgesia should be considered.

The use of another NSAID is not recommended. Consider appropriate washout times when switching from one NSAID to another or when switching from corticosteroid use to NSAID use.

**INFORMATION FOR DOG OWNERS:** Carprive Injection, like other drugs of its class, is not free from adverse reactions. 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 decreased appetite, vomiting, diarrhea, dark or tarry stools, increased water consumption, increased urination, pale gums due to anemia, yellowing of gums, skin or white of the eye due to jaundice, lethargy, incoordination, seizure, or behavioral changes. **Serious adverse reactions associated with this drug class can occur without warning and in rare situations result in death (see Adverse Reactions). Owners should be advised to discontinue Carprive Injection therapy and contact their veterinarian immediately if signs of intolerance are observed.** The vast majority of patients with drug related adverse reactions have recovered when the signs are recognized, the drug is withdrawn and veterinary care, if appropriate, is initiated. Owners should be advised of the importance of periodic follow up for all dogs during administration of any NSAID.

**ADVERSE REACTIONS:** There were no serious adverse events reported during clinical field studies for the injectable formulation. The following categories of abnormal health observations were reported.

Percentage of Dogs with Abnormal Health Observations Reported in Clinical Field Studies with the Injectable

Observation*	carprofen (n=168)	Placebo (n=163)
Vomiting	10.1	9.2
Diarrhea/Soft stool	2.4	3.7
Dermatitis	0.6	1.2
Dysrhythmia	0.6	0.6
Swelling	0	1.2
Dehiscence	1.2	0
WBC increase	13.7	6.7

\*A single dog may have experienced more than one occurrence of an event.

Post-Approval Experience:

Although not all adverse reactions are reported, the following adverse reactions are based on voluntary post-approval adverse drug experience reporting. The categories of adverse reactions are listed by body system.

**Gastrointestinal:** Vomiting, diarrhea, constipation, inappetence, melena, hematemesis, gastrointestinal ulceration, gastrointestinal bleeding, pancreatitis.

**Hepatic:** Inappetence, vomiting, jaundice, acute hepatic toxicity, hepatic enzyme elevation, abnormal liver function test(s), hyperbilirubinemia, bilirubinuria, hypoalbuminemia. Approximately one-fourth of hepatic reports were in Labrador Retrievers.

**Neurologic:** Ataxia, paresis, paralysis, seizures, vestibular signs, disorientation.

**Urinary:** Hematuria, polyuria, polydipsia, urinary incontinence, urinary tract infection, azotemia, acute renal failure, tubular abnormalities including acute tubular necrosis, renal tubular acidosis, glucosuria.

**Behavioral:** Sedation, lethargy, hyperactivity, restlessness, aggressiveness.

**Hematologic:** Immune-mediated hemolytic anemia, immune-mediated thrombocytopenia, blood loss anemia, epistaxis.

**Dermatologic:** Pruritus, increased shedding, alopecia, pyotraumatic moist dermatitis (hot spots), necrotizing panniculitis/vasculitis, ventral ecchymosis. In rare situations, injection site reactions including necrosis, abscess and seroma formation, and granulomas have been reported with the injectable formulation.

**Immunologic or hypersensitivity:** Facial swelling, hives, erythema. In rare situations, death has been associated with some of the adverse reactions listed above. To report a suspected adverse reaction call Norbrook at 1-866-591-5777.

**ANIMAL SAFETY:** Clinical field studies were conducted on 331 dogs undergoing orthopedic or soft tissue surgery. Dogs were administered 2 mg/lb of carprofen subcutaneously two hours prior to surgery and once daily thereafter, as needed, for 2 days (soft tissue surgery) or 3 days (orthopedic surgery). The type and severity of abnormal health observations in carprofen- and placebo-treated animals were approximately equal and few in number (see Adverse Reactions). Changes in clinicopathologic indices of hematopoietic, renal, hepatic, and clotting function were not clinically significant. The mean post-treatment serum ALT values were 8.4 IU and 7.0 IU less than pre-treatment values for dogs receiving carprofen and placebo, respectively. The mean post-treatment AST values were 1.5 IU and 0.7 IU greater for dogs receiving carprofen and placebo, respectively. Swelling and warmth were associated with the injection site after subcutaneous administration of carprofen injectable. Long term use of the injectable has not been studied.

Norbrook Laboratories Limited,  
Newry, BT35 6PU, Co. Down,  
Northern Ireland.  
101 NOV 2014



resultant fibrosis. Esophageal diverticula and esophageal neoplasias are rare in dogs and cats. Vascular ring anomalies, usually noted when the young animal begins eating solid food, require surgery to correct, as does a hiatal hernia. Causes of cricopharyngeal achalasia are unclear, and fluoroscopy is necessary for diagnosis. Megaesophagus can be congenital or acquired, and diagnosing the underlying cause is critical to successful treatment.—*Burgener IA*

### Sedation as an Alternative to General Anesthesia in Pet Birds

Sedation should be considered in place of general anesthesia in birds that are stressed, ill, debilitated, or in respiratory distress. In cases in which general anesthesia is unnecessary, sedation can help with restraint and stress-reduction. Midazolam, a benzodiazepine sedative, can reduce anxiety but has no analgesic effect. Butorphanol, a widely used opioid analgesic, has proven safe in some healthy psittacine species. Suggested doses are 1-3 mg/kg of butorphanol with 0.25-1.0 mg/kg of midazolam by IM injection. Onset is rapid (within 2-3 minutes); length of sedation ranges 20 minutes to several hours. Response is

variable, from mild to profound (often in debilitated patients). Sedation can be useful for cases in which handling produces stress, vocalizations, and increased heart and respiratory rates. Birds in respiratory distress often show improvement in rate and effort with sedation, likely because of decreased anxiety. Although general anesthesia is necessary to completely eradicate patient movement, good quality radiographs can be obtained with sedation in many patients. Lidocaine and bupivacaine are local analgesic agents that can be used at a dose of 1-2 mg/kg each for procedures causing mild-to-moderate discomfort. Sedation plus local analgesia can be used to obtain vascular access or to place intraosseous catheters, as well as for cleansing and wound debridement, abscess lancing, or digit amputation. Although further studies to help determine therapeutic dose ranges as well as safety and efficacy data are needed, sedation use in psittacines has not been associated with increased patient mortality.—*Lennox AM ■ cb*

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- Same active ingredient, formulation and dosing regimen as Rimadyl® (carprofen) Injectable
- For relief of pain and inflammation associated with osteoarthritis (OA) and for control of postoperative pain associated with soft tissue and orthopedic surgeries in dogs
- Reduces treatment costs
- Dose once or twice daily

Observe label directions. For subcutaneous use in dogs only. Do not use in cats. As with other NSAIDs, rare but serious side effects involving the digestive system, kidneys or liver may occur. Such signs may be serious, resulting in hospitalization or even death. Regular monitoring is required for pets on medication. Pet owners should be advised to discontinue use if side effects occur and contact their veterinarian. See product labeling for full product information.

**FOR VETERINARY USE ONLY** See page 82 for product information summary.

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**ELEANOR C. HAWKINS**, DVM, DACVIM, is assistant department head for the small animal internal medicine and emergency/critical care service at North Carolina State University. Her clinical, research, and teaching interest is in respiratory disease. Author of the respiratory section of the *Small Animal Internal Medicine* textbook, Dr. Hawkins has been section editor of *Current Veterinary Therapy* and *The 5-Minute Veterinary Consult*. She has served as board chair of the American College of Veterinary Internal Medicine. CONSULTANT ON CALL PAGE 69



**REBECCA A. JOHNSON**, DVM, PhD, DACVAA, is clinical associate professor at the anesthesia and pain management section at University of Wisconsin School of Veterinary Medicine. Her interests include the changes in normal respiratory neurophysiology associated with anesthetic drugs and disease states.

A graduate of The Ohio State University, Dr. Johnson completed a residency at University of Wisconsin, where she also completed a PhD in respiratory neurophysiology. MEDICATIONS PAGE 65



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physiology and DVM from The Ohio State University. MAKE YOUR DIAGNOSIS PAGE 41



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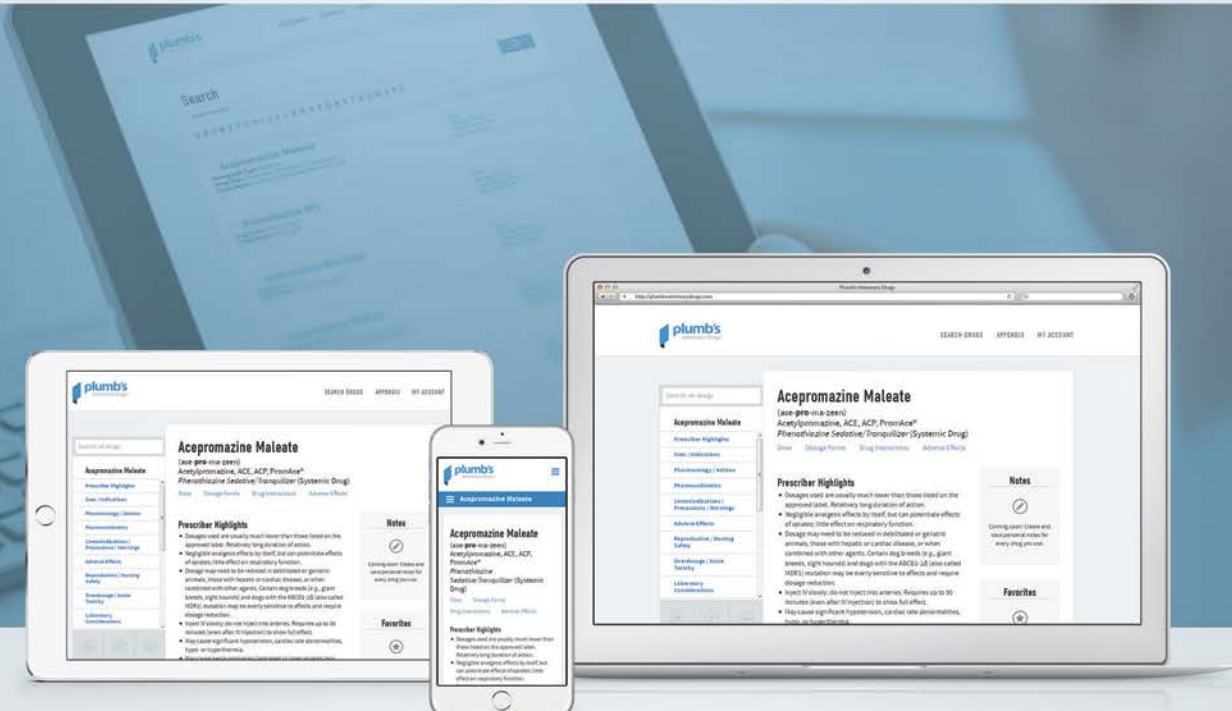
DIAGNOSTIC TREE PAGE 18



**MARK TROXEL**, DVM, DACVIM, (Neurology), is staff neurologist and neurosurgeon at Massachusetts Veterinary Referral Hospital in Woburn. He is creator and publisher of NeuroPetVet (neuropetvet.com), an online veterinary neurology teaching site. His interests

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continues on page 86



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OUR AUTHORS continued from page 84



**ALEXANDER WERNER**, VMD, DACVD, is editor of the dermatology section of the *5-Minute Veterinary Consult* textbook and co-author of the *Small Animal Dermatology Clinical Companion*, 2nd edition. He practices at the Animal Dermatology Center in Studio City and Westlake Village, California, and Reno, Nevada. He serves on the *Clinician's Brief* advisory board. CLINICAL VIEW

PAGE 8



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## Quiz Yourself on this issue's features

### CLINICAL VIEW page 8

- Which of the following has NOT been associated with feline plasma cell pododermatitis (FPP)?
  - FIV-positive status
  - Breed
  - Food hypersensitivity
  - Seasonal waxing and waning
  - All of the above have been associated with FPP

### CLINICAL VIEW page 10

- Later radiographic signs of pano-steitis include an increase in \_\_\_\_\_ within the medullary cavity of long bones and loss of the \_\_\_\_\_ pattern.

### APPLIED BEHAVIOR page 15

- The primary goal in treating dogs that growl is to eliminate the growling behavior.
  - True
  - False

### DIAGNOSTIC TREE page 18

- In middle-aged to older dogs weighing more than 15 kg, what is the most likely differential diagnosis for a left apical systolic heart murmur?

- Mitral valve degeneration
- Ventricular septal defect
- Dilated cardiomyopathy
- (A) and (C)

### CONSULTANT ON CALL page 23

- Peracute to acute neurologic clinical signs that continue to progress after 24 hours suggest that a patient has suffered a stroke.
  - True
  - False

### PROCEDURES PRO page 29

- Upon completion of Ehmer sling placement, the crus should be:
  - Abducted and flexed, with slight internal rotation
  - Abducted and flexed, with slight external rotation
  - Adducted and flexed, with slight internal rotation
  - Adducted and flexed, with slight external rotation

### CUTTING EDGE page 35

- Gene therapy in the treatment of veterinary cardiac disease may be possible for diseases for which a \_\_\_\_\_ has been identified.

### MAKE YOUR DIAGNOSIS page 41

- To prevent *Brucella canis* from entering a kennel, serologic testing should be performed on all new arrivals, followed by \_\_\_\_\_ weeks of quarantine and then retesting.
  - 4
  - 8
  - 12
  - 16

### MEDICATIONS page 65

- Administration of \_\_\_\_\_ after administration of dexmedetomidine increases the risk of dysrhythmias.

### CONSULTANT ON CALL page 69

- Which of the following findings would rule out a diagnosis of bacterial pneumonia?
  - Normal CBC
  - Normal body temperature
  - Absence of crackles on lung auscultation
  - None of the above

Answer key: 1: B 2: mineral density, trabecular bone 3: B 4: D 5: B 6: A 7: genetic mutation 8: B 9: anticholinergics 10: D

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We asked...

**Which of the following rehabilitation methods are among those offered patients at your clinic?**

You answered...

- |  |     |
|--|-----|
| A. Hydrotherapy .....                          | 11% |
| B. Acupuncture .....                           | 16% |
| C. Agility training (cavaletti poles) .....    | 2%  |
| D. Passive range of motion .....               | 26% |
| E. We use 2 or more of the above methods ..... | 45% |

This month's question...

**Which feline presentation haunts you the most?**

- Missed string foreign body/string under the tongue
- Missed abdominal mass
- Missed foreign body
- I don't really worry about that stuff

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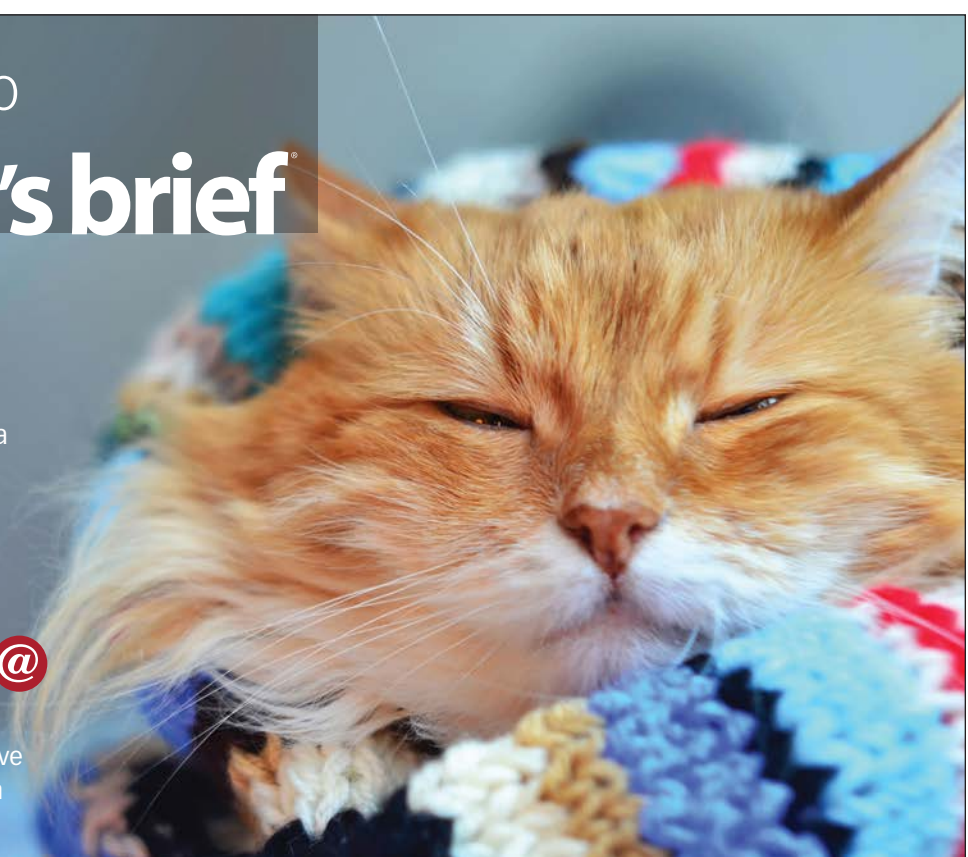


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