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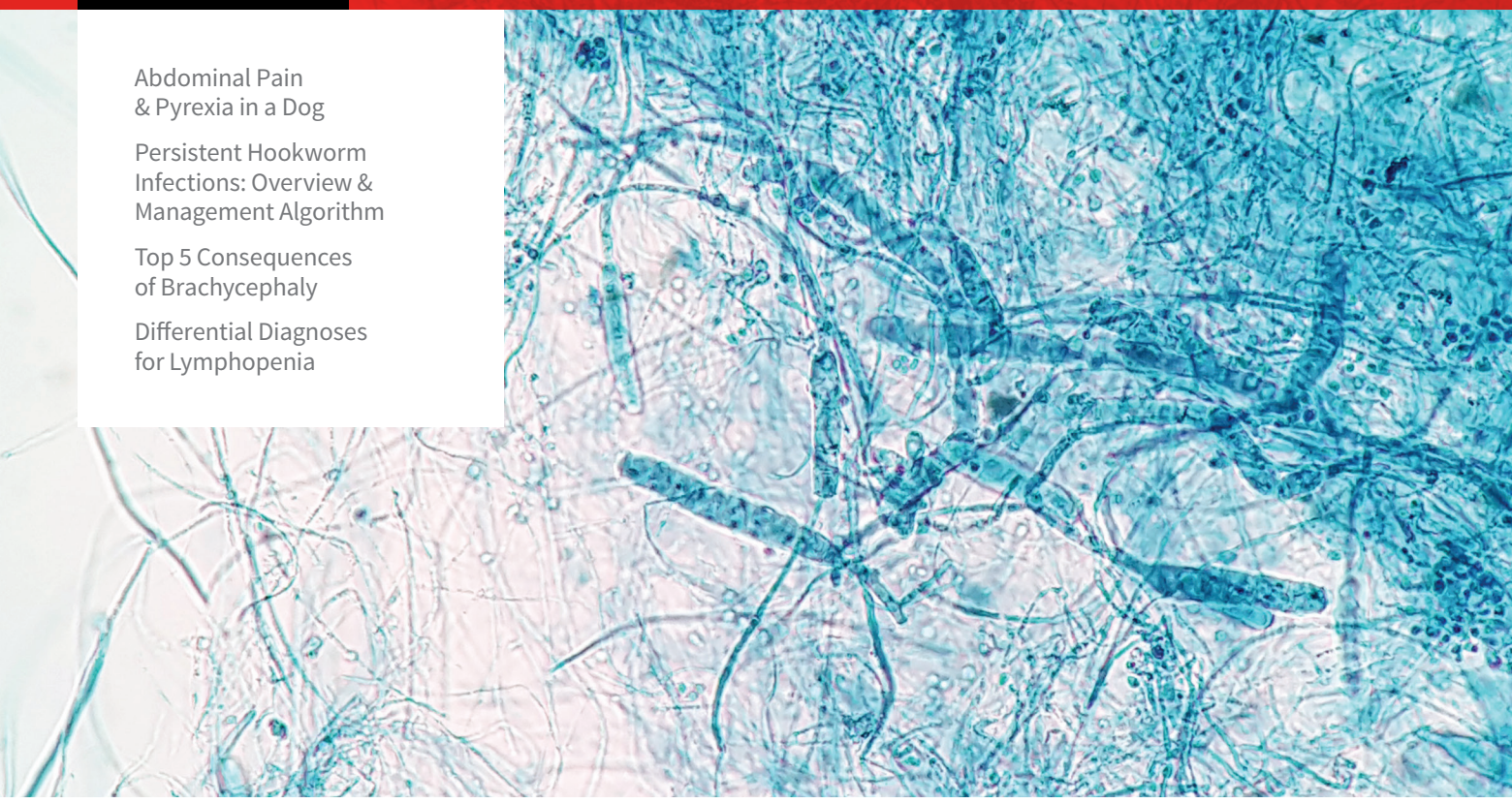

Volume 18 Number 8

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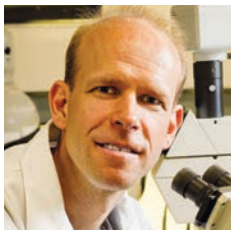

EDITOR IN CHIEF
J. SCOTT WEESE
DVM, DVSc, DACVIM
dr.weese@briefmedia.com
Professor
Ontario Veterinary College
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CHIEF VETERINARY OFFICER & EDITOR
INDU MANI
DVM, ScD
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OUR AUTHORS

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

DIFFERENTIAL DIAGNOSIS PAGE 41

PABLO DAVID JIMENEZ CASTRO, DVM, is currently completing his PhD in the Department of Infectious Diseases at University of Georgia. He earned his DVM from the National University of Colombia in Bogotá, Colombia, before working at Novartis Animal Health and Elanco Animal Health in regulatory affairs. Dr. Castro's research interests include clinical efficacy and safety trials, anthelmintic resistance, and the epidemiology and control of parasites of veterinary and public health importance. His work has been published in several peer-reviewed journals, and he has given presentations at various scientific meetings.

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CONSULT THE EXPERT PAGE 61

ANNE FAWCETT, BVSc, MVS, MANZCVS (Animal Welfare), DECAWBM (AWSEL), is a lecturer at The University of Sydney in Australia and a companion animal veterinarian. She coauthored *Veterinary Ethics: Navigating Tough Cases*, coedited *The Vet Cookbook*, and has written numerous peer-reviewed journal articles and book chapters. Dr. Fawcett is a member of the leadership council of the Humane Society Veterinary Medical Association, in Gaithersburg, Maryland.

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RAY M. KAPLAN, DVM, PhD, DEVPC, DACVM (Parasitology), is a professor in the Department of Infectious Diseases at University of Georgia. He earned his DVM from Virginia–Maryland College of Veterinary Medicine and worked in a mixed-species practice before earning his PhD in veterinary parasitology from University of Florida. Dr. Kaplan's research program is focused on measuring, understanding, and solving problems of drug resistance in nematode parasites. He is a past president of the American Association of Veterinary Parasitologists and has received the Pfizer Award for Research Excellence and the American Association of Veterinary Parasitologists–Boehringer Ingelheim Distinguished Veterinary Parasitologist Award.

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CONSULT THE EXPERT PAGE 61

KAREN A. MORIELLO, DVM, DACVD, is a clinical professor emerita of veterinary dermatology at University of Wisconsin–Madison. Dr. Moriello earned her DVM from University of Illinois and completed a residency at University of Florida. Her clinical research interests include the treatment and management of feline dermatophytosis. She is a former coeditor of the journal *Veterinary Dermatology*.

CONSULT THE EXPERT PAGE 30

ARIADNA RIBAS LATRE, DVM, DECVIM, MRCVS, is a specialist in internal medicine at Dick White Referrals in Six Mile Bottom, Cambridgeshire, where she also completed a residency in internal medicine and earned her European diploma in internal medicine. She earned her DVM from Autonomous University of Barcelona and completed a rotating internship in a referral hospital in Barcelona, Spain, where she developed an interest in internal medicine. Dr. Ribas Latre has worked in emergency and first opinion practices, and she completed externships in internal medicine, critical care, and imaging in several referral centers before completing a rotating internship at University of Liverpool in England.

CASE IN POINT PAGE 11

From *Clinician's Brief* on Social Media

WE ASKED . . .

What is the most unique gift you have received from a pet owner?

"A Christmas cookie box, during the Christmas season, filled with a week's worth of individually wrapped cat turds that the owner wanted to show me"—*Michelle L*

"An aloe plant; the owner said I had healing properties like the plant. I was very touched."—*Stephanie L*

"Toilet paper. We were excited because it was right when toilet paper was in short supply in stores."—*Jazmin A*

"A clock made in the shape of a cat" —*Nina T*

"A tin of spam and a frozen turkey" —*Louise T*

How do you answer when pet owners ask, "What would you do if it was your pet?"

"I usually tell them, 'I can't tell you because it's not my pet.' Then I review their options to see what is still unclear and to find what best fits their personal situation."—*Lilian V*

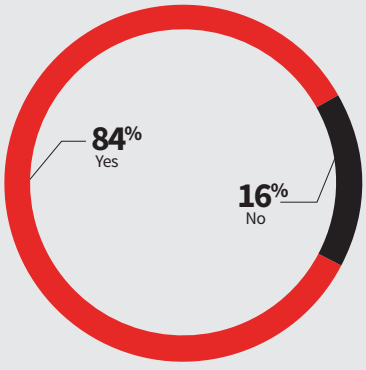
"I give an honest answer of what I would do in that moment, knowing I may never face a similar situation because I practice preventive care and early intervention with my pets. However, I try to imagine what it is like being in their shoes, and I always finish by saying, 'But I'll support whatever decision you make, and I'll try to make the best of it for your pet, whatever the decision is. This is your pet.'"—*Angel B*

"I always tell the truth, even if it is sad."—*Ekatherina S*

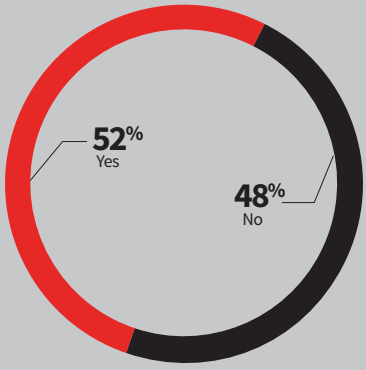
"I tell them I cannot answer because everyone's circumstances are different." —*Stan G*

"That question is the bane of my existence."—*Patreece L*

Have you had an increase in patient load since the pandemic started?



Do you give vaccines to patients that also had a spay or neuter procedure that day?



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Dermatophytosis
Karen A. Moriello, DVM, DACVD

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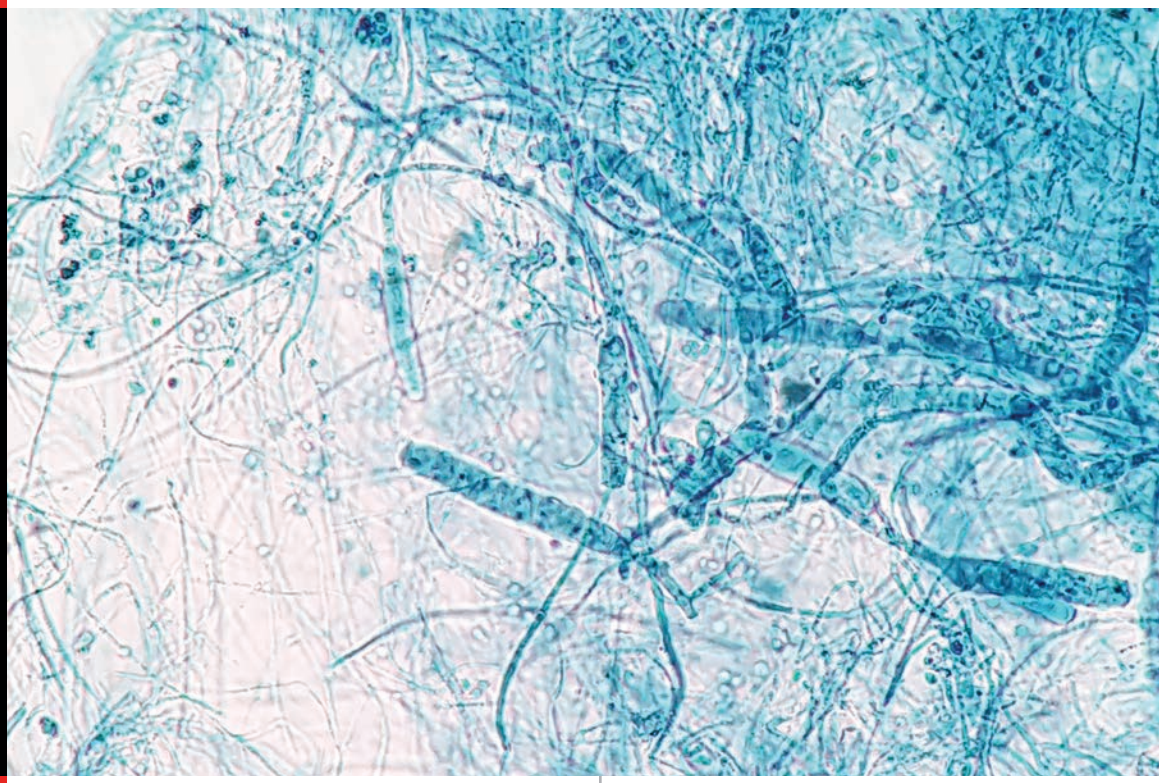

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Mark M. Smith, VMD, DACVS, DAVDC, AVDC and ACVS Founding Fellow of Oral & Maxillofacial Surgery

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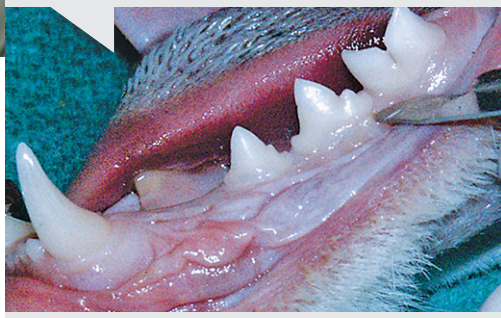

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References: 1. Data on file, Study Report No. C863R-US-12-018, Zoetis Inc. **2.** Gonzales AJ, Humphrey WR, Messamore JE, et al. Interleukin-31: its role in canine pruritus and naturally occurring canine atopic dermatitis. *Vet Dermatol*. 2013;24(1):48-53. doi:10.1111/j.1365-3164.2012.01098.x. **3.** Data on file, Study No. 16SORDER0101, Zoetis Inc.

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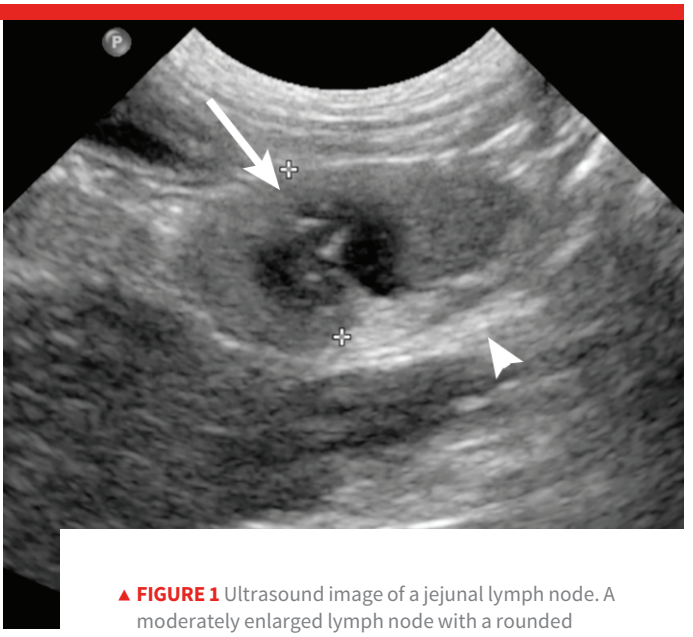
Abdominal Pain & Pyrexia in a Cairn Terrier

Ariadna Ribas Latre, DVM, DECVIM, MRCVS
Dick White Referrals
Six Mile Bottom, Cambridgeshire



▲ **FIGURE 1** Ultrasound image of a jejunal lymph node. A moderately enlarged lymph node with a rounded heterogeneous appearance and ill-defined hypoechoic patches can be seen (***arrow***). The mesenteric fat around the lymph node was diffusely hyperechoic (***arrowhead***).

Ruby, a 3-year-old, 15.6-lb (7.1-kg) spayed cairn terrier, was presented for a 24- to 36-hour history of hyporexia and abdominal pain. She had no previous medical conditions, vaccinations and flea and tick preventives were up to date, and she had not traveled outside the United Kingdom. Initial assessment revealed pyrexia (rectal temperature, 103.8°F [39.9°C]). She was started on potentiated amoxicillin (20 mg/kg SC) and referred to a specialty clinic for further evaluation.

Physical Examination

On presentation, Ruby was lethargic but alert and responsive. Abdominal pain, pyrexia, and hyporexia were of main concern. Her BCS was 5/9, her rectal temperature was 104.4ºF (40.2ºC), and she was ≈7% dehydrated. She demonstrated apparent generalized discomfort on abdominal palpation. No peripheral lymphadenopathy was noted, and the rest of the physical examination was unremarkable.

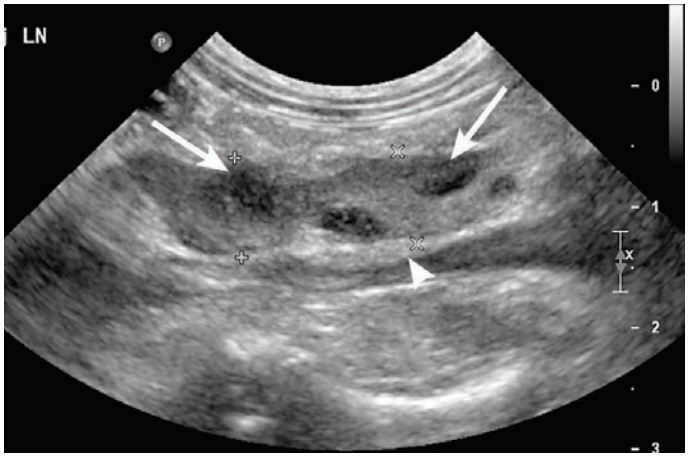
Diagnostics

Differential diagnoses for abdominal pain should include any infectious, inflammatory, or neoplastic disease that affects the abdominal organs; rupture, volvulus, or obstruction of an abdominal organ; and referred pain from other muscular, neurologic, or bony structures. Differential diagnoses for pyrexia should include drug administration; toxin ingestion; and infectious, inflammatory/immune-mediated, and neoplastic disease. Differential diagnoses for hyporexia are broad and can be related to abdominal pain or pyrexia; however, other causes may include primary GI or systemic disease; local disease affecting structures involved in prehension, mastication, or swallowing (ie, oral, dental, muscular, bone, neurologic conditions); pain; and behavior.[1]

CBC and serum chemistry profile revealed a moderate neutrophilic leukocytosis (23,300/µL; reference

interval, 3,000-11,500/µL) without toxic changes. The remaining CBC and serum chemistry results were within normal limits. C-reactive protein (CRP) levels were also assessed for systemic inflammation, and levels were markedly elevated at 29.4 mg/dL (reference interval, <1).

Abdominal ultrasonography revealed the presence of multiple enlarged, heterogeneous, and rounded cranial mesenteric lymph nodes (***Figures 1***, previous page, and ***2***). These findings were suggestive of round cell neoplasia, lymphadenitis (infectious or noninfectious), or reactive lymphadenopathy. There was a small amount of free abdominal fluid, which was sampled and submitted for analysis; this was compatible with a nonseptic suppurative exudate. Culture results of the fluid were negative. Fine-needle aspirates and cytology of the abdominal lymph nodes were consistent with neutrophilic lymphadenitis (***Figure 3***). No infectious agents were seen. The rest of the abdominal ultrasound was unremarkable.



▲ **FIGURE 2** Ultrasound image of a jejunal lymph node. A moderately enlarged lymph node with a lobulated heterogeneous appearance and ill-defined hypoechoic patches can be seen (***arrows***). The mesenteric fat around the lymph node was diffusely hyperechoic (***arrowhead***).

TREATMENT AT A GLANCE

- Glucocorticoid treatment can be started after infectious causes have been excluded.
- Most patients seem to respond to glucocorticoid therapy, and rapid resolution of clinical signs is associated with resolution of lymphadenopathy.
- Immunosuppressive glucocorticoids are often necessary to control clinical signs.
- Other immunosuppressive medications may be needed if patient response is suboptimal or steroid adverse effects are severe.

Differential diagnoses for neutrophilic lymphadenitis include infectious disease, immune-mediated disease, neoplasia, and sterile lymphadenitis.[2] Thoracic radiography was performed to assess for any distant cause of infection, neoplasia, or inflammation, but the results were unremarkable. Urinalysis was unremarkable, urine culture was negative, and serology for arthropod-borne disease (eg, *Ehrlichia* spp, *Anaplasma* spp, *Borrelia* spp) was negative.

Ultrasound-guided trucut biopsies of the abdominal lymph nodes were submitted for histopathology and culture to exclude infectious lymphadenitis. Histopathology confirmed neutrophilic lymphadenitis (***Figure 4***), and lymph node tissue cultures (bacterial and fungal) were negative.

DIAGNOSIS:
STERILE STEROID-RESPONSIVE NEUTROPHILIC LYMPHADENITIS

Treatment

Ruby was initially treated with IV crystalloid fluid therapy for dehydration and opioid pain relief (methadone at 0.2 mg/kg every 4 hours) for abdominal discomfort. Antibiotic therapy with potentiated amoxicillin was continued.

Because an infectious cause was not found, treatment with glucocorticoids was started (prednisolone at 1.5 mg/kg every 24 hours). Ruby remained normothermic 48 hours after treatment was initiated; she had a good appetite and there was no evidence of abdominal pain. She was discharged, and treatment with glucocorticoids was continued.

Recheck examinations were scheduled to occur every 3 to 4 weeks. Ruby remained clinically well, and her CRP levels normalized (0.4 mg/dL; reference interval, <1). Repeat CBC also revealed resolution of the inflammatory leukogram. Glucocorticoid treatment was gradually decreased by 25% to 30% every 3 to 4 weeks, on condition that clinical signs remained resolved and physical examination was normal. Abdominal ultrasonography was performed 1 month after initial diagnosis, revealing resolution of the mesenteric lymphadenopathy.

Prognosis & Outcome

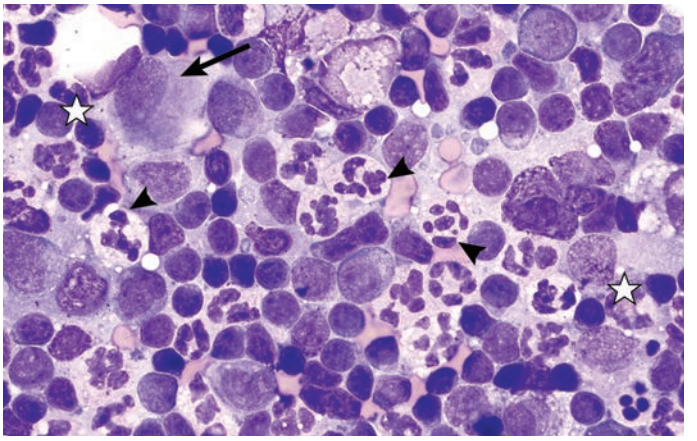
Treatment with glucocorticoids was discontinued ≈4 months after diagnosis because the patient remained clinically well. Ruby remained healthy without treatment 2.5 years after initial presentation.

Discussion

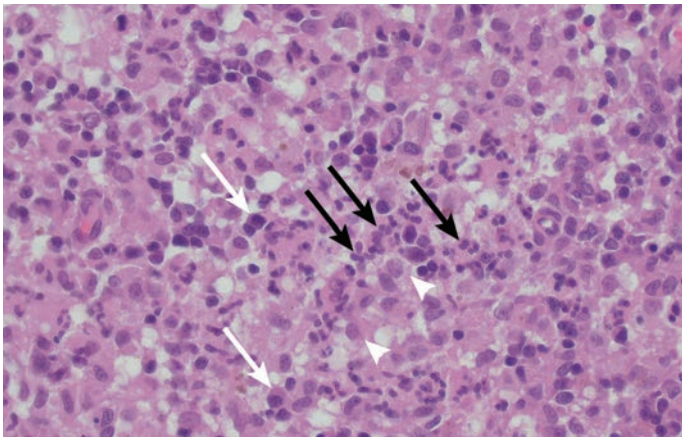
Sterile steroid-responsive lymphadenitis (SSRL) is not well-characterized in dogs; however, it should be considered in dogs with pyrexia of unknown origin and inflammatory lymphadenopathy for which no underlying cause can be found.

There is little information available about SSRL. Two retrospective, multicentric studies discussed this condition (including clinical signs, diagnostic approach, and treatment) in different breeds,[3] particularly in English springer spaniels.[4] Other case reports/series have also reported on SSRL, especially in English springer spaniels with or without concurrent dermatologic signs.[5-8]

A diagnosis of SSRL can be determined via cytology and/or histopathology by documenting an inflammatory infiltrate in lymph nodes without evidence of infectious agents or other underlying disease. It is key that infectious causes be excluded before SSRL is diagnosed; geographic variations are important considerations in these cases, as prevalence of infectious disease can vary depending on the region or country. Good clinical response is initially seen in most patients after glucocorticoid initiation, but other immunosuppressants can be



▲ **FIGURE 3** Cytology of a fine-needle aspirate from a jejunal lymph node revealing large numbers of variably degenerate neutrophils (***arrowheads***). No bacteria were observed. Small numbers of macrophages (***arrow***) and small and medium lymphocytes (***stars***) were present. These changes are compatible with neutrophilic lymphadenitis. *Magnification 100×*



▲ **FIGURE 4** Hematoxylin and eosin stained histologic image of a trucut biopsy from a jejunal lymph node. Normal lymph node architecture was effaced by the presence of sheets of degenerate neutrophils (***black arrows***) and smaller numbers of macrophages (***arrowheads***) and plasma cells (***white arrows***). *Magnification 40×*

CRP = C-reactive protein

SSRL = Sterile steroid-responsive lymphadenitis

considered if patient response is suboptimal or steroid adverse effects are severe. Relapses are possible after discontinuation of therapy, so monitoring may be necessary.[3,4] CRP evaluation has been used as a monitoring technique. Young female dogs, particularly English springer spaniels, seem to be predisposed to lymphadenitis.[3,4] Previous reports of lymphadenitis in English springer spaniels included a case of sterile neutrophilic-macrophagic lymphadenitis associated with nodular panniculitis,[6] granulomatous necrotizing lymphadenitis,[7] and mineral-associated lymphadenopathy.[8]

SSRL should be on the differential diagnosis list for young adult dogs presented with pyrexia and lymphadenopathy.

CRP = C-reactive protein
SSRL = Sterile steroid-responsive lymphadenitis

TAKE-HOME MESSAGES

- SSRL should be considered in dogs that have pyrexia and variable degrees of lymphadenopathy.
- Clinical signs can vary.
- Definitive diagnosis of SSRL involves extensive investigation to rule out detectable underlying infectious, inflammatory, or neoplastic causes.
- Lymphadenopathy can be external, internal, or both.
- Young female dogs, particularly English springer spaniels, seem to be predisposed.[3,4]
- CRP can be used for monitoring purposes.
- Relapses are possible.

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LOOK FOR THESE ARTICLES IN FUTURE ISSUES

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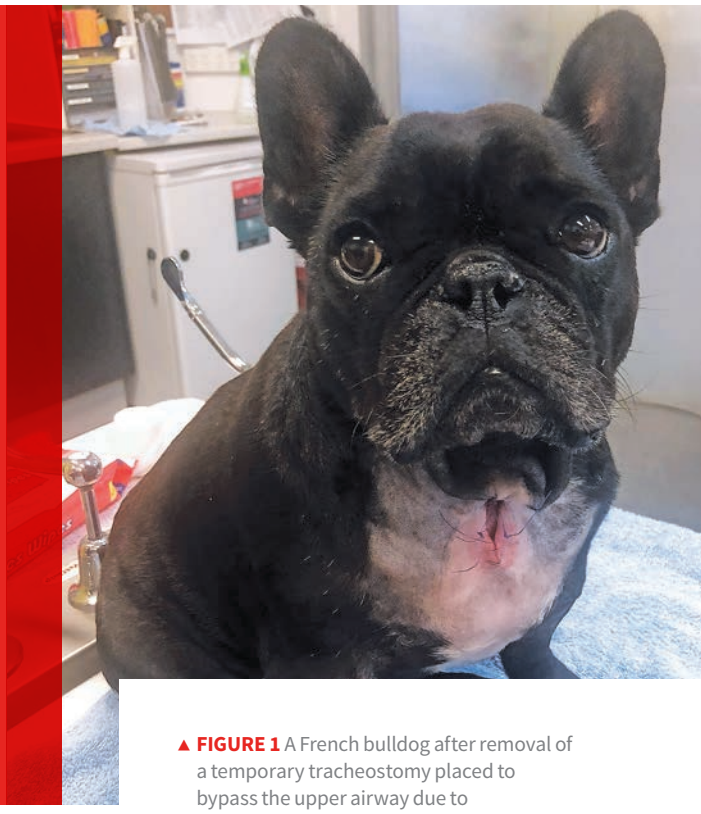
RenalTech is the first of a new generation of predictive diagnostic tools poised to ensure veterinary care continues to develop parallel to human healthcare. The ability to predict disease offers veterinarians a powerful, tangible way to inspire pet owner compliance with personalized care plans that maintain pet quality of life and the bond between pet owners and their pets.

Top 5 Consequences of Brachycephaly

Anne Fawcett, BVSc, MVS, MANZCVS (Animal Welfare), DECAWBM (AWSEL)
The University of Sydney
Sydney, Australia



▲ **FIGURE 1** A French bulldog after removal of a temporary tracheostomy placed to bypass the upper airway due to obstruction triggered by severe heat stress. Some dogs require a permanent tracheostomy. *Image courtesy of Dr. Ellie Leister, Veterinary Specialist Services*

Brachycephaly (ie, shortening of the facial skeleton) is characteristic of some dog breeds (eg, French bulldogs, English bulldogs, pugs, Cavalier King Charles spaniels, Pekingese, Boston terriers). Brachycephalic conformation is associated with multiple health problems, some of which can be life-threatening and most of which are lifelong. Despite widespread publicity about these problems, popularity of these breeds as pets continues to increase.[1] Awareness of the consequences of brachycephaly is important when advising pet owners about breed selection, advising breeders, and mitigating consequences for affected dogs. It should be noted that some syndromes are more common and/or severe in some brachycephalic breeds.

Following are the top 5 consequences of brachycephaly according to the author.

1 Brachycephalic Obstructive Airway Syndrome

Shortening of the facial skeleton leads to crowding and compression of the upper airway, resulting in upper airway resistance that increases the work of breathing and leads to air

TOP 5 CONSEQUENCES OF BRACHYCEPHALY

1. Brachycephalic Obstructive Airway Syndrome
2. Conditions Associated with Skeletal Abnormalities
3. Dental Disease
4. GI Disease
5. Ocular & Ophthalmologic Disease

hunger during exertion; this syndrome is known as brachycephalic obstructive airway syndrome (BOAS).[2] Anatomically, brachycephaly is associated with stenotic nares, hypertrophy of nasal turbinates, an elongated and thickened soft palate, a thickened tongue, everted laryngeal saccules, everted palatine tonsils, and a hypoplastic trachea; this can lead to partial or complete airway obstruction.[3] Clinical signs range from mild stridor to severe dyspnea and collapse. Affected dogs may experience sleep apnea.[4,5] Increased airway resistance can also result in soft tissue swelling and laryngeal collapse, exacerbating BOAS and potentially causing complete obstruction of the upper airway, necessitating emergency opening of the airway (***Figure 1***, previous page).[6,7]

Because owners are often unaware that BOAS indicates underlying pathology, and because upper airway noises may be considered normal for the breed, there can be delays in seeking veterinary care.[8] Clinicians should advise owners on when to seek veterinary care and educate them on the sensitivity of brachycephalic breeds to heat stress (***Figure 2***).[9]

▲ **FIGURE 2** A bulldog with hyperthermia (body temperature, 107°F [41.5°C]) at an outdoor event. The dog was first cooled in tepid water then transported to a critical care facility. Brachycephalic dogs are prone to heat stress due to upper airway obstruction (ie, increasing inspiratory workload) and ineffective evaporative cooling.

Early surgical correction is recommended to minimize progression of airway pathology in BOAS patients.[10,11] Surgery typically addresses stenotic nares, elongated soft palate, everted laryngeal saccules, and palatine tonsils. Care must be taken when anesthetizing brachycephalic dogs with BOAS because of increased risk for complications (eg, regurgitation, aspiration pneumonia, respiratory distress).[12,13] Perioperative administration of a prokinetic and a histamine blocker, minimal use of opioids, and recovery in an intensive care unit reduced the incidence of postoperative regurgitation in brachycephalic dogs.[13]

2 Conditions Associated with Skeletal Abnormalities

Chiari-like malformation of the skull and craniocervical junction is most commonly seen in Cavalier King Charles spaniels, Brussels Griffons, and affenpinschers. Compression of neural tissue and disruption of CSF circulation can result and lead to development of fluid-filled cavities in the spinal cord (ie, syringomyelia [ie, neck scratcher's disease]).[14] Affected dogs may have concurrent ventriculomegaly,[3] a painful condition most commonly seen in smaller brachycephalic breeds.[14]

Abnormalities of the vertebral column, including spondylosis deformans and vertebral malformations (eg, hemivertebrae), predispose brachycephalic dogs to intervertebral disk disease.[15] Brachycephalic screw-tailed dogs (eg, French bulldogs, pugs, English bulldogs) are more commonly affected by spinal malformations, including kyphosis and scoliosis, which can increase the risk for intervertebral disk disease.[3]

Prognosis for affected dogs varies according to the severity of the underlying abnormality. Medical management with analgesic and anti-inflammatory drugs may relieve signs in mildly affected dogs. Surgery may be of benefit for some dogs; however, the prognosis is poor for dogs with marked scoliosis, intractable spinal pain, and/or neurologic signs refractory to medical management.[3]

3 Dental Disease

Brachycephaly is associated with dental malocclusion, overcrowding, and misalignment of teeth. A number of brachycephalic breeds have mandibular mesioclusion (ie, an undershot jaw), which is specified in breed standards; for example, French bulldog breed standards include an underjaw that is deep, square, broad, undershot, and well turned up.[16]

Malocclusion is associated with difficulty chewing food, temporomandibular joint dysfunction, trauma to soft tissue of the oral cavity, and premature tooth loss.[17] Brachycephaly may also predispose dogs to dentigerous cysts, supernumerary incisors, and rotated, fused, or unerupted teeth (***Figure 3***).[18] Some brachycephalic breeds (eg, boxers, bulldogs) may have prominent palatal rugae, in which plaque, hair, and food become trapped, leading to inflammation and development of granulomas; surgical correction may be required.[18] Dental radiography is essential in the diagnosis and management of dentigerous cysts and supernumerary teeth. Owners should be advised to maintain dental hygiene and pursue regular dental examinations for their pet.

4 GI Disease

Brachycephalic dogs are at increased risk for GI disease, including hiatal hernia, gastroesophageal reflux, esophagitis, delayed esophageal transit time, and redundant esophagus.[19,20] French bulldogs have a higher incidence of hiatal hernia as compared with other dogs.[20] Brachycephalic dogs presented with regurgitation and/or dysphagia are more likely to have esophageal motility disorders as compared with nonbrachycephalic dogs.[21] Clinical signs of GI disease (eg, dysphagia, vomiting, regurgitation) are common in brachycephalic dogs with clinical upper respiratory tract disease.[19] Of note, GI lesions were seen endoscopically in brachycephalic dogs that did not have GI signs.

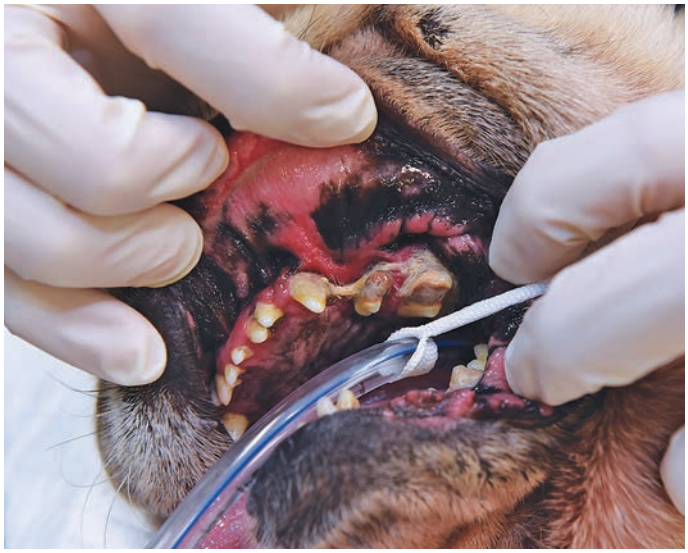
Surgical management of respiratory disease may reduce GI signs.[19,20] Because patients with hiatal hernia and esophageal disease are at greater risk for esophagitis and aspiration during and after anesthesia, patients with a history of regurgitation or reflux require close monitoring, and owners should be advised of increased risks.

5 Ocular & Ophthalmologic Disease

Brachycephalic breeds may have a variety of conformational defects (eg, medial canthal entropion, trichiasis, inappropriate tear fluid drainage leading to epiphora, qualitative and/or quantitative tear deficiencies, shallow orbits, proptosis, reduced corneal sensitivity) that compromise ocular health.[22] These abnormalities increase the risk for ocular disease (including corneal ulcerations and erosions, vascular keratitis, pigmentary keratitis, corneal fibrosis, and keratoconjunctivitis sicca), leading to pain and vision deficits.[22] Brachycephalic dogs are 11 to 20 times more likely to be affected by corneal ulcers than are nonbrachycephalic dogs.[23,24] Nasal folds, visible sclera, and an increased eyelid aperture have been identified as risk factors.[23]

BOAS = brachycephalic obstructive airway syndrome

Continues ▶



▲ **FIGURE 3** Oral cavity of a pug undergoing dental treatment. A rotated premolar and carnassial tooth, marked gingival recession and gingivitis, marked plaque and calculus, and fur entrapment can be seen.

In some cases, surgical management (eg, medial canthoplasty) can reduce the risk for corneal exposure and irritation. Medical and surgical management may be required to manage acute and chronic conditions (eg, corneal ulceration). Careful attention should be paid to the ocular conformation of these dogs during examination so that owners can be advised accordingly.

Conclusion

Brachycephalic conformation predisposes dogs to respiratory, neurologic, dental, GI, ocular, and other disorders—including dermatologic abnormalities. Because these conditions affect the health and welfare of dogs, it is important they are not dismissed as normal for the breed.

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IMPORTANT SAFETY INFORMATION: Use with caution in dogs with a history of seizures. Simparica Trio contains sarolaner, a member of the isoxazoline class, which has been associated with neurologic adverse reactions including tremors, ataxia, and seizures in dogs with or without a history of neurologic disorders. The safe use of Simparica Trio has not been evaluated in breeding, pregnant, or lactating dogs. The most frequently reported adverse reactions in clinical trials were vomiting and diarrhea. **See Brief Summary of full Prescribing Information on page 22.**

**Amblyomma americanum, Amblyomma maculatum, Dermacentor variabilis, Ixodes scapularis,* and *Rhipicephalus sanguineus.*
†Toxocara canis, Toxascaris leonina, Ancylostoma caninum, and *Uncinaria stenocephala.*

ZOETIS PETCARE

Brief Summary of full Prescribing Information.

Simparica TRIO™

(sarolaner, moxidectin, and pyrantel chewable tablets)

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
SIMPARICA TRIO is indicated for the prevention of heartworm disease caused by *Dirofilaria immitis* and for the treatment and control of roundworm (immature adult and adult *Toxocara canis* and adult *Toxascaris leonina*) and adult hookworm (*Ancylostoma caninum* and *Uncinaria stenocephala*) infections. SIMPARICA TRIO kills adult fleas (*Ctenocephalides felis*) and is indicated for the treatment and prevention of flea infestations, and the treatment and control of tick infestations with *Amblyomma americanum* (lone star tick), *Amblyomma maculatum* (Gulf Coast tick), *Dermacentor variabilis* (American dog tick), *Ixodes scapularis* (black-legged tick), and *Rhipicephalus sanguineus* (brown dog tick) for one month in dogs and puppies 8 weeks of age and older, and weighing 2.8 pounds or greater.

DOSAGE AND ADMINISTRATION
SIMPARICA TRIO is given orally once a month, at the recommended minimum dose of 0.54 mg/lb (1.2 mg/kg) sarolaner, 0.011 mg/lb (24 µg/kg) moxidectin, and 2.27 mg/lb (5 mg/kg) pyrantel (as pamoate salt).

Dosage Schedule

Body Weight (lbs)	Sarolaner per Tablet (mg)	Moxidectin per Tablet (mg)	Pyrantel per Tablet (mg)	Number of Tablets Administered
2.8 to 5.5	3	0.06	12.5	One
5.6 to 11.0	6	0.12	25	One
11.1 to 22.0	12	0.24	50	One
22.1 to 44.0	24	0.48	100	One
44.1 to 88.0	48	0.96	200	One
88.1 to 132.0	72	1.44	300	One
>132.0	Administer the appropriate combination of tablets			

SIMPARICA TRIO can be offered to the dog with or without food.

Care should be taken to ensure that the dog consumes the complete dose and that part of the dose is not lost or refused. If a dose is missed, give SIMPARICA TRIO immediately and resume monthly dosing.

Heartworm Prevention:
SIMPARICA TRIO should be administered at monthly intervals year-round or at least within one month of the animal's first seasonal exposure to mosquitoes and continuing until at least 1 month after the dog's last seasonal exposure. If a dose is missed, give SIMPARICA TRIO immediately and resume monthly dosing. When replacing a monthly heartworm preventive product, SIMPARICA TRIO should be given within one month of the last dose of the former medication.

Flea Treatment and Prevention:
Treatment with SIMPARICA TRIO may begin at any time of the year. SIMPARICA TRIO should be administered year-round at monthly intervals or started at least one month before fleas become active.

To minimize the likelihood of flea re-infestation, it is important to treat all dogs and cats within a household with a flea control product.

Tick Treatment and Control:
Treatment with SIMPARICA TRIO can begin at any time of the year. SIMPARICA TRIO should be administered year-round at monthly intervals or started at least one month before ticks become active.

Intestinal Nematode Treatment and Control:
For the treatment of roundworm (immature adult and adult *Toxocara canis* and adult *Toxascaris leonina*) and adult hookworm (*Ancylostoma caninum* and *Uncinaria stenocephala*) infections, SIMPARICA TRIO should be administered once as a single dose. Monthly use of SIMPARICA TRIO will control any subsequent infections.

CONTRAINDICATIONS
There are no known contraindications for the use of SIMPARICA TRIO.

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

Keep SIMPARICA TRIO in a secure location out of reach of dogs, cats and other animals to prevent accidental ingestion or overdose.

PRECAUTIONS
Sarolaner, one of the ingredients in SIMPARICA TRIO, is a member of the isoxazoline class. This class has been associated with neurologic adverse reactions including tremors, ataxia, and seizures. Seizures have been reported in dogs receiving isoxazoline class drugs, even in dogs without a history of seizures. Use with caution in dogs with a history of seizures or neurologic disorders.

Prior to administration of SIMPARICA TRIO, dogs should be tested for existing heartworm infections. Infected dogs should be treated with an adulticide to remove adult heartworms. SIMPARICA TRIO is not effective against adult *D. immitis*.

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

ADVERSE REACTIONS
In a field safety and effectiveness study, SIMPARICA TRIO was administered to dogs for the prevention of heartworm disease. The study included a total of 410 dogs treated once monthly for 11 treatments (272 treated with SIMPARICA TRIO and 138 treated with an active control). Over the 330-day study period, all observations of potential adverse reactions were recorded. The most frequent reactions reported in the SIMPARICA TRIO group are presented in the following table.

Table 1. Dogs with Adverse Reactions

Clinical Sign	SIMPARICA TRIO *n* = 272	Active Control *n* = 138
Vomiting	14.3%	10.9%
Diarrhea	13.2%	8.0%
Lethargy	8.5%	6.5%
Anorexia	5.1%	5.8%
Polyuria	3.7%	3.6%
Hyperactivity	2.2%	0.7%
Polydipsia	2.2%	2.9%

In a second field safety and effectiveness study, SIMPARICA TRIO was administered to 278 dogs with fleas. Adverse reactions in dogs treated with SIMPARICA TRIO included diarrhea.

In a third field safety and effectiveness study, SIMPARICA TRIO was administered to 120 dogs with roundworms. Adverse reactions in dogs treated with SIMPARICA TRIO included diarrhea and vomiting.

For a copy of the Safety Data Sheet or to report adverse reactions, call Zoetis Inc. at 1-888-963-8471. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or www.fda.gov/reportanimalae.

STORAGE CONDITIONS
Store at or below 30°C (86°F).

HOW SUPPLIED
SIMPARICA TRIO is available in six flavored tablet sizes (see **DOSAGE AND ADMINISTRATION**). Each tablet size is available in packages of one, three, or six tablets.

Approved by FDA under NADA # 141-521

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Nutraceuticals: Where Are We Today?

Approximately 40% of pet owners have considered using alternative medical therapies, and ≈90% of clinicians sell food or supplements containing a novel ingredient (eg, herbs, botanicals, nutraceuticals that contain compounds endogenous to animals). Most common supplements address joint function and predominantly include glucosamine, followed by fish oil, probiotics, lysine, milk thistle, and *S*-adenosyl methionine. These compounds may be regulated as either food or drugs depending on the stated intended use. Lack of regulation contributes to issues regarding safety, efficacy, and manufacturing.

There are no mandates that regulate labeling, including contents, assurances in manufacturing, or directions for use. Safety concerns are related to adverse effects of the active ingredient or excipients, contaminants, and/or therapeutic failure, especially in cases in which traditional therapy has been overlooked. There is no effective reporting system in place. Dosages are often empiric rather than based on scientific studies that address product chemistry, proposed mechanism of action, and pharmacokinetics. The impact of drugs on dietary supplements is limited due to lack of mandated safety studies, limited clinical trials, questionable quality of products, and wide diversity of compounds. The most clinically relevant pharmacokinetic interactions described with regard to dietary supplements reflect inhibition or induction of absorption or metabolism.

One useful site to evaluate these compounds is ConsumerLab.com. This for-profit organization tests supplements per the manufacturer's request for properly labeled strength, lack of contaminants, and other information.
—*Boothe DM*

Elimination Trials in Food Allergic Dogs: A Critical Appraisal

Differences between food allergies and intolerances are not always clear, as the pathogenesis and incidence of true food allergy is unknown. In dogs, the primary sign of food hypersensitivity is nonseasonal pruritus with dermatitis patterns similar to atopic dermatitis; patients may also be presented with otitis externa and/or GI signs.

Diagnosis can be challenging due to false positives and negatives on serum allergy tests. Improvement of clinical signs when fed a novel protein diet is considered the gold standard for diagnosis. Challenges include choosing a diet, cross reactions between meat sources in a species, and common exposure to table scraps. Trace levels of allergens in over-the-counter dog foods make prescription novel protein diets necessary. Alternatively, hydrolyzed diets may be less likely to be allergenic.

Flavored medications should be avoided during food trials. Novel diet trials should last a minimum of 6 weeks; improvement may continue for ≤8 to 10 weeks. All other clinical signs (eg, ear infection, superficial pyoderma) should be treated simultaneously; however, this can affect trial length. After signs have been resolved for 2 to 3 weeks, the patient may be rechallenged with the original diet. Dogs with food allergy often show signs of relapse within 2 weeks, and dogs with immunoglobulin E-mediated food allergy can develop signs within hours.—*Banovic F*

Acute Intoxications: When & How Should IV Lipid Emulsions Be Used?

IV lipid emulsion (ILE) use in the treatment of various lipophilic drug toxicities and in veterinary toxicology has greatly expanded. ILE has a long shelf life (ie, ≤2 years) and is relatively affordable, making it a valuable alternative for lipophilic toxicosis, in which ILE can be used in combination with GI decontamination or when GI decontamination procedures are not possible or are unsuccessful. ILE should only be considered to treat toxicosis from lipophilic agents associated with life-threatening clinical signs or lethal doses. Toxicoses that have been successfully treated with ILE include local anesthetics, moxidectin, ivermectin, permethrin, NSAIDs, baclofen, marijuana, cholecalciferol, bromethalin, tremorgenic mycotoxins, methamphetamine, and calcium-channel blockers.

Although the mechanism of action of ILE is not yet known, several theories have been presented. The lipid sink theory is most widely accepted and postulates that circulating lipid emulsions provide a compartment into which lipophilic drugs partition, accelerating their movement toward organs responsible for metabolism and secretion and sparing target organs. An alternative theory proposes that ILE has a direct effect on myocardial cells, thereby improving cardiac output.

ILE should be administered via IV catheter (peripheral or central) with an initial bolus of 1.5 mL/kg over 2 to 5 minutes, followed by a CRI of 0.25 mL/kg/minute for 30 to 60 minutes. If the patient does not improve or if the patient relapses, readministration can be considered. The maximum total dose is 16.5 mL/kg/hour. Adverse effects are rare, but ILE interferes with all lipophilic drugs, including those used to treat the patient. Currently, only 2 cases documenting adverse effects have been reported, both of which involved cats that developed corneal lipidosis following ILE treatment that resolved without intervention.—*Wulrod V*

IV lipid emulsion should only be considered to treat toxicosis from lipophilic agents associated with life-threatening clinical signs or lethal doses.

Nutrition & GI Syndrome in Rabbits

Rabbit GI syndrome (RGIS) includes trichobezoars, gastric stasis, and GI hypomotility/ileus. Many pet rabbits are fed a low-fiber diet that is the main contributing factor of RGIS. Additional factors include a small relatively non-distensible muscular pyloric sphincter, inability to vomit, consumption of hair during grooming, stress, pain, and disease. In rabbits, dietary fiber primarily stimulates gut motility rather than serving as a source of nutrition. The ideal pelleted hay diet consists of 15% to 16% crude fiber and 16% crude protein. Grass hays (eg, timothy, prairie, oat) are recommended, as they are higher in fiber and lower in protein and calcium than are legume hays (eg, alfalfa). Pellets should be supplemented with loose hay fed ad libitum. Fresh vegetables, small amounts of fresh fruit (eg, strawberries, apples), and dark, fibrous, leafy greens may also be supplemented.

Signs of RGIS include anorexia, oligodipsia, reduced number and size of fecal pellets, diarrhea, a distended and tender dough-like stomach, and signs of pain (eg, hunched stance, teeth grinding). Acute obstructions can lead to shock and require emergency decompression; however, most cases can be managed with aggressive supportive care and medication, including parenteral fluids, force feeding, rehydration of stomach contents, and stimulation of GI motility. Broad-spectrum antibiotics may be required for suspected clostridial overgrowth and endotoxemia. Analgesics and/or simethicone can ease abdominal pain. Abdominal massage, gentle exercise, stress reduction, and supplemental heat can also aid in recovery. Patients treated at home typically have a faster recovery time. Surgical intervention is rarely necessary for chronic cases and generally carries a poorer prognosis. —*Carpenter JW*

Feline Constipation: Getting Crap out of a Cat

Constipation in cats can progress to obstipation and megacolon, rendering constipation a potentially serious, sometimes terminal, disease. There are many possible causes of constipation, and it may not be initially recognized by pet owners. Vomiting, decreased appetite, and lethargy may be more apparent to the owner than an obvious change in stools. Clinical history is crucial and should include clinical course, environmental conditions, and litter box arrangement. A thorough physical examination should include assessment of body weight, muscle condition, neurologic status, and hydration. Examination of the perianal area should include anal sacs, hip joints, colonic palpation, and rectal examination. Dehydration secondary to other illness is a common cause of feline constipation. Mechanical obstruction, functional obstruction, medication, and obesity are other general causes. Diagnostic testing includes CBC, serum chemistry profile, urinalysis, total thyroxine (T_4), and abdominal radiography (possibly followed by a radiography contrast study, abdominal ultrasonography, CT, or MRI).

Dehydration must be treated IV, SC, PO, or via feeding tube. Specific therapy includes warm water retention enemas (5-10 mL/kg 2-3 times over 12-24 hours) and, sometimes, gentle manual extraction of stool. Laxatives—classified as lubricating, emollient, stimulating, or bulk-forming—may be useful and can be administered as part of the enema. More recently, polyethylene glycol (6-10 mL/kg/hour) has been administered by trickling through a nasoesophageal tube; this method may require 12 to 18 hours, but the success rate and minimally invasive nature of the procedure make it worth considering. After constipation has resolved, management may include oral lactulose, dietary fiber, and prokinetics (eg, cisapride at 5 mg/cat PO every 8-12 hours). One commercially available psyllium-enriched dry extruded veterinary diet has shown promise for management of these patients.—*Webb CB*

PRACTICE HOTLINE

The latest in products & services

Vaccination Guidelines for Latin American Companion Animal Practitioners

New guidelines for vaccination against infectious diseases in the Latin American region have been released by the **WSAVA** (**wsava.org**) Vaccination Guidelines Group (VGG). The guidelines are the result of a 4-year project and include an overview of the veterinary profession and veterinary education in the region, as well as an evidence-based review of companion animal infectious diseases in Latin America, including rabies virus infection and canine visceral leishmaniosis.

These guidelines were produced following visits by the VGG team to Argentina, Brazil, and Mexico; analysis of a questionnaire completed by 1,390 respondents in 5 Latin American countries; discussions with key opinion leaders in the region; and a comprehensive review of published scientific literature.

Responses to 70 frequently asked questions are also provided, as well as current information on local product availability, licensed duration of immunity, and the incorporation of vaccination as part of an annual health check program. This latest document accompanies similar guidelines produced by the VGG for Asia and the WSAVA Global Vaccination Guidelines, which offer evidence-based best practice recommendations on vaccinations for companion animal veterinarians globally; all are available for free download at **bit.ly/2CN0yGM**. *—Press Release 6/20*

Helping Clinics Promote Pet Diabetes Month

Merck Animal Health, **Purina**, and **Zoetis** formed the Diabetes Pet Care Alliance program in 2014, with the goal of facilitating the screening of >2,000 pets during Pet Diabetes Month. The Diabetes Pet Care Alliance encourages patient screening, pet owner education, and early intervention for dogs and cats with diabetes, which could lead to a positive prognosis. The program gives clinicians access to tools and resources to raise diabetes awareness in owners and increase the number of pets screened for the disease.

Owners with pets diagnosed with diabetes can receive free kits to help begin management of their pet's diabetes. Program kits include the following:

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- 10-mL vial of Vetsulin (porcine insulin zinc suspension) from Merck Animal Health

Enrollment is September 1 to October 31, 2020; owners with pets diagnosed from November 1 to December 31, 2020, are eligible to receive the free kits. Enrollment information is available at **usa.petdiabetesmonth.com**.*—Press Release 7/20*

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Canine Otitis Externa & the Importance of Ear Cleaning

ARDEN KLINCZAR, DVM | DERMATOLOGY RESIDENT | ANIMAL DERMATOLOGY CLINIC | MARIETTA, GEORGIA

Otitis externa, or inflammation of the external ear canal, is common in small animal practice.[1] Routine ear cleaning is an essential part of maintaining a favorable ear environment and keeping ears healthy in dogs prone to otitis externa.[1-4]

Understanding the causes and factors contributing to development of otitis externa is critical to successful management.[2-4] Causes may directly induce inflammation (primary causes [eg, allergy or endocrine disease]) or lead to disease in abnormal ears (secondary causes [eg, yeast or bacterial overgrowth, overcleaning]).[1-7] Predisposing factors such as conformation of the ear are present before disease develops, and perpetuating factors such as edema or proliferative changes to the ear canal and changes in the tympanic membrane occur as a result of inflammation and can prevent resolution.[1,7] Once identified, primary causes should be addressed, secondary infections resolved, and predisposing and perpetuating factors managed.[1,7]

THE ROLE OF EAR CLEANING

Ear cleaning is an important part of managing otitis externa and should be performed routinely in dogs prone to otitis externa to prevent recurrence.[3,6,7] When performed well, ear cleaning helps maintain a normal ear environment by removing debris, microbes, small foreign bodies, and biofilm that could result in otitis externa.[6,8] By eliminating exudate and debris, a proper assessment of the ear canal and the tympanic membrane can be performed and the inactivation of some antimicrobials by inflammatory material prevented.[6] Ear cleaning is beneficial in dogs with inflamed ears secondary to allergies, seborrheic ears with excessive cerumen production, and/or stenotic or pendulous ears in which normal epithelial migration is impeded.[6-8]

EAR CLEANING TECHNIQUES

Several cleaning techniques (eg, manual cleansing, bulb syringes, ear flushing) can be used.[1,6] Ear wash or rinse is the most common method used at home; this technique should be clearly demonstrated to the owner to ensure effective cleaning. When performed poorly, ear cleaning can cause trauma, ongoing inflammation, and discomfort, leading to decreased compliance.[7]

To prevent maceration and secondary infection, ear cleaning should generally be performed every 48 hours.[6] Follow-up examinations are important to assess whether the ears are being cleaned effectively or whether the owner should receive better instructions or employ a new technique.

EAR CLEANING PRODUCTS

Many ear cleaning solutions with different active ingredients are available.[1,6,7] The clinician should understand the purpose of each ingredient to recommend the appropriate product.[1,3] It is important that no harm is caused when using an ear cleanser, particularly in ears with a ruptured tympanic membrane. Saline and water should be used in patients without intact tympanic membranes, as many ear cleaning solutions are potentially ototoxic.[6] Ear cleansers may be used more frequently in certain circumstances (eg, infected ears) or less frequently if used as maintenance to prevent recurrence.

Antimicrobials

Some ear cleaners, such as those with chlorhexidine or tris-EDTA, have been shown to have antimicrobial activity, which may be due to active ingredients or a low pH.[9-11] Products like these can limit bacterial and yeast proliferation, helping prevent recurrent infections.[12,13]

Ceruminolytics

Ceruminolytics emulsify waxes and lipids, which are then more readily flushed from the ear,[1,6] and are commonly used to break up waxy or purulent debris prior to ear flushing or other cleaning under sedation.[6,7,14,15] Ceruminolytics can be ototoxic if left in the middle ear; flushing with water or saline after use may decrease the chance of ototoxicity.

Astringents

Astringents are used to dry ears and prevent maceration and secondary infection.[6,7] They are often combined with ceruminolytics and surfactants in drying/cleaning products but can be used as sole therapy.[6,7] Common astringent ingredients such as isopropyl alcohol, boric acid, benzoic acid, and salicylic acid can be useful after the ear has been cleaned or prophylactically after bathing, swimming, or the application of aqueous-based solutions in dogs prone to otitis.[6-8]

Some ceruminolytics and astringents can cause pain when used in sensitive ears.[6] Choosing a nonirritating formula for maintenance use is essential to prevent complications and improve compliance. EPIOTIC® Advanced Ear Cleanser is cleanser that breaks down wax and has astringent properties, with a neutral pH and nonirritating formula. With once to twice daily use, EPIOTIC® Advanced Ear Cleanser has been shown to reduce microbial adhesion and work as well as acidic cleaners, with no noted adverse effects.[6,9,16]

CONCLUSION

Effective ear cleaning plays an essential part in otitis externa by helping to manage inflammation and infection that can lead to more complicated otic disease. The product chosen should be based on the individual patient and the underlying causes and factors at play. Demonstrating proper application of the ear cleanser for the owner can help prevent trauma and ongoing inflammation of the canal, which can inhibit resolution of otitis. Frequent follow-up and ongoing training for owners is important to ensuring good compliance and long-term outcomes.

For references, please see **cliniciansbrief.com/article/canine-otitis-externa-importance-ear-cleaning**

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DERMATOPHYTOSIS

Karen A. Moriello, DVM, DACVD
University of Wisconsin–Madison

Dermatophytosis (ie, ringworm) is a superficial fungal disease of the skin, hair, and claws that affects 1% to 4% of cats and dogs worldwide.[1]

Background & Pathophysiology

The most common dermatophyte pathogens in small animals are *Microsporum canis*, *M gypseum*, and *Trichophyton* spp.[1] *M gypseum* is found in and contracted from soil; *Trichophyton* spp are presumably transmitted through contact with large animals or rodents.[1]

Dermatophytosis is more common in warm, humid climates and is seasonal in temperate climates.[1] The primary risk factor is exposure to another infected animal. Group housing of animals (eg, pet shops, animal shelters, animal rescue situations, hoarding) can also increase risk for disease.[1]

Successful development of an infection nidus requires exposure of the skin surface to a critical load of infective spores (ie, arthrospores), increased moisture on the skin surface to facilitate sporulation, and microtrauma. The latter is believed to be important in facilitating infection, as experimental infections in cats have been difficult to establish without it.[1] Under optimal conditions, infective spores can adhere to skin within 6 hours, germinate within 24 hours, and begin shedding within 7 days.[1] Lesion foci are detectable within 7 days; however, pet owners may not notice lesions until 14 to 21 days postexposure.[1]

The primary mode of transmission is via direct contact with an infected animal. Transmission can also be from contaminated fomites, especially those that can cause microtrauma (eg, clipper blades, grooming tools, collars).

Transmission via a contaminated environment has been shown to be inefficient in establishing active lesions.[1] In the author's experience, exposure to a contaminated environment most commonly results in culture-positive, lesion-free fomite carriage; however, this exposure can be a risk factor for transmission if the patient is debilitated, has chronic skin issues, and/or has any inflammatory skin disease.

History

Patients of all ages and breeds can be affected, but young animals and those under severe physiologic stress are predisposed.[1] Persian cats, Yorkshire terriers, and Jack Russell terriers appear to be overrepresented; subcutaneous nodular lesions have been observed almost exclusively in Persian cats and Yorkshire terrier dogs.[1] Working and hunting dogs are predisposed to kerion lesions, which are focal areas of dermatophytosis that resemble nodular draining lesions of deep pyoderma.[1]

Clinical history of dermatophytosis is variable. A history of skin lesions in a patient recently adopted from a high-risk situation should raise suspicion. Owners may also report skin lesions on other animals in the home and/or on themselves.

Clinical Signs

Hair loss, scaling, crusting, and erythema are the most common clinical lesions. Lesions tend to be asymmetric and can affect any area on the body but often appear first on the face, ears, and distal extremities. Lesions may be difficult to find in long-haired animals. Facial lesions appearing as pustular dermatophytosis (ie, resembling pemphigus foliaceus) are rare. Lesions may be focal, multifocal, or widespread, and disease may be mild to severe; presentation reflects the health of the host.

Pruritus may be present and is highly variable; some lesions may be intensely pruritic and exudative and may resemble superficial pyoderma in dogs or exudative eosinophilic lesions in cats.

Nodular inflammatory lesions may be observed in dogs or cats, especially working dogs; nodular lesions in cats may be exudative or subcutaneous.

Purulent paronychia may be observed. Concurrent bacterial infection may worsen clinical signs.

Diagnosis

Although dermatophytosis is a differential diagnosis for any inflammatory follicular disease, it is more commonly diagnosed in kittens and puppies and less frequently diagnosed in adult animals. In adult dogs, superficial pyoderma, demodicosis, and

other ectoparasitic infestations that can cause hair loss, erythema, and/or scaling should be ruled out. In adult cats, flea infestation, flea allergy dermatitis, and other infestations and allergies associated with generalized scaling should be ruled out.

Dermatophytosis and pemphigus foliaceus can have similar presentations in adult animals and can be differentiated by histopathology, cytology, direct examination of hairs, and fungal culture.

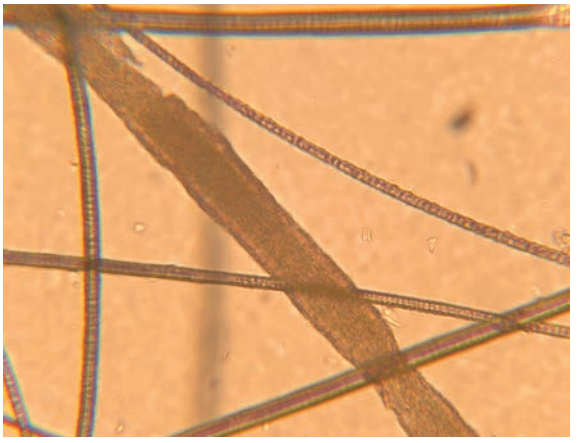
No gold-standard diagnostic test is available for dermatophytosis.[1] Histopathology (± tissue culture) can confirm nodular or pustular dermatophytosis, but fungal culture must be performed to determine fungal species (see ***Point-of-Care Diagnostics***). In a study, direct microscopic examination of hairs (ie, trichogram) and skin scrapings from lesions confirmed infection in >85% of cases.[1] Fungal culture can be used to identify spores on the hair coat and confirm disease if the sample is from a lesion site. Positive fungal cultures from whole-body toothbrush samples may be due to true disease or fomite carriage; thus, sampling should be limited to lesion sites. Dermatophyte PCR is sensitive and specific for fungal DNA but detects both viable and nonviable fungal DNA.[1] PCR has a quicker turnaround time than does fungal culture, but laboratory access may be limited. Field studies comparing fungal culture and PCR are few, so it is not possible to comment on how concordant results are between the tests. If PCR is pursued, a large number of hairs and crusts only from the target lesions should be submitted to the laboratory. A toothbrush fungal culture should also be sent to the laboratory in case it is needed to confirm the infection. The author's first choice is a fungal culture.

Point-of-Care Diagnostics

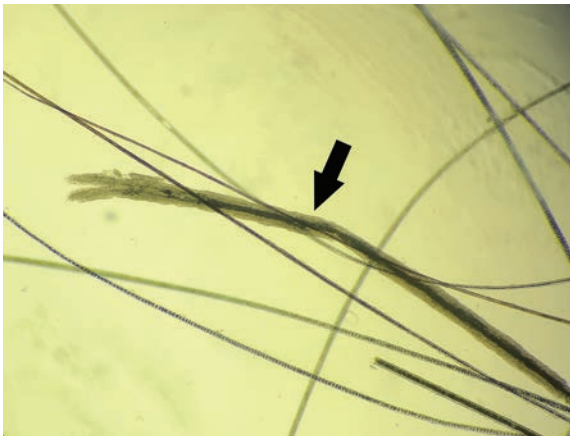
Microscopic Examination of Hairs

Hairs should be plucked in the direction of growth and skin scrapings obtained from the lesion margins. Mineral oil should be used for mounting. Clearing agents used to soften nail keratin in human medicine (eg, potassium hydroxide) are not needed and can add artifacts or damage microscope lenses, as they are caustic. Cover slips should be placed on slide specimens and viewed at 4× and 10× magnification. Infected hairs are wider and paler in appearance, and ectothrix spores cuffing the hair may be present (***Figures 1*** and ***2***).

Wood's lamp examination is recommended when dermatophytosis is suspected. This is not a diagnostic test but rather a diagnostic tool that helps find



▲ **FIGURE 1** Microscopic view of an infected hair wider than normal hairs; internal structures of the hair shaft are not visible. *10× magnification. Image courtesy of Dr. Karen A. Moriello*



▲ **FIGURE 2** Microscopic view of a newly infected hair wider than surrounding hairs; some internal structures (eg, dark black pigment; ***arrow***) are visible on the proximal part of the hair. *4× magnification. Image courtesy of Dr. Karen A. Moriello*

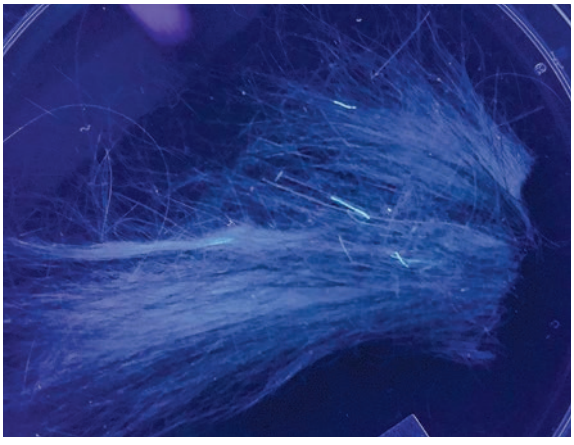
suspect *M canis*-infected hairs for direct examination. In recent studies, 91% to 100% of patients with untreated spontaneous infections showed positive fluorescence.[1] Historic studies reporting 30% to 50% positive fluorescence were from retrospective laboratory studies and not from in vivo studies.

A plug-in Wood's lamp with a wavelength of 320 to 400 nm and built-in magnification should be used. During examination, the clinician should hold the lamp 2 to 4 cm from the patient's skin and proceed slowly, starting at the head. Apple-green fluorescence on the hair shaft is suggestive of *M canis* infection. Crusts do not glow and may need to be lifted (***Figure 3***) to find infected hairs underneath.

If infection is confirmed with point-of-care diagnostics, treatment can be initiated.

Fungal Culture

Fungal culture can be performed via point-of-care or laboratory diagnostics. The most commonly used fungal culture medium is dermatophyte test medium (DTM). If fungal culture is performed in-house, easy-open or petri dish-type plates with the largest surface area possible should be used. Fungal culture jars can be difficult to inoculate, are prone to increased bacterial overgrowth due to increased humidity, and can be difficult to obtain samples from the surface. Removing media from the jars is not recommended, as this increases exposure to a possible pathogen.



▲ **FIGURE 3** Wood's lamp examination of hairs. The classic apple-green fluorescence of *M canis*, the only important veterinary pathogen that fluoresces, can be noted. *Image courtesy of Dr. Karen A. Moriello*

An untreated lesion should be sampled using a soft-bristled toothbrush, which is mycologically sterile if prepackaged. It is important to sample the skin surface and hairs; materials will be entrapped in toothbrush bristles. Crusts can be gently lifted to sample beneath them using the edge of a skin scraping spatula or other blunt-edged instrument.

In-house fungal cultures can be performed on site, and one study showed that the difference in results between point-of-care testing and a reference laboratory was <3% if proper procedures were followed.[2] In-house testing practices should follow laboratory biohazard practices.

Fungal cultures should be incubated at room temperature and examined daily; darkness is not necessary. *M canis* cultures can be finalized at day 14 if no growth is observed.[3,4] Studies have not been conducted for *M gypseum,* but this pathogen is not difficult to isolate, and it is reasonable to extrapolate studies from *M canis* to this pathogen. Regarding *Trichophyton* spp, a study in humans examined 5549 samples and found only 16 required >17 days of incubation, and only 1 of 16 was a veterinary pathogen (*T mentagrophtyes*).[3,4] The authors concluded 17 days is adequate for finalizing a diagnosis for human pathogens.[4]

Microscopic identification must be performed to confirm diagnosis (see ***Suggested Reading***, page 38). Pale, flat, and fluffy gross colonies should be sampled for microscopy. If DTM is used, clinicians should look for pale colonies with a red color change in the medium around them as they grow. It is important to remember that the red color change is *not* diagnostic of a dermatophyte. Colony morphology may also be suggestive of a positive fungal culture, but it is not diagnostic; microscopic identification is always needed.

Treatment & Management

In otherwise healthy animals, dermatophytosis usually self-resolves; treatment is intended to shorten the course of disease and limit contagion. Owners should be informed that dermatophytosis is a non-life–threatening zoonotic disease that causes easily treatable skin lesions and be instructed to consult their personal physician if they have questions or suspect they may have skin lesions. Misinformation regarding cleaning, disinfection, and environmental contamination is pervasive; owners should be advised that fungal spores do not invade home surfaces as do other molds (eg, mildew), do not cause respiratory disease, and can be easily removed.

Owners should also be informed that treatment is multimodal and includes reasonable confinement, cleaning, topical therapy, systemic therapy, and monitoring.

Confinement

Confinement of patients limits the area that requires cleaning and helps prevent the spread of disease. Confinement alone is not curative and should be implemented with care to ensure the welfare of the patient; the area should be a single room large enough to allow eating, sleeping, and exercise.

Dermatophytosis can occur in young animals during key socialization and bonding times; owners should continue to socialize and play with the infected pet. Owners should wear gloves and washable clothing and avoid direct skin-to-skin contact. Hand hygiene is important; owners should wash hands or use hand sanitizer (found to be sporicidal in the author's laboratory) if soap and water are not available. Safe, washable, interactive toys should be provided. Recommendations for other animals in the home are similar to those for any infectious disease: Direct contact should be avoided, and bowls, brushes, leashes, and bedding should not be shared among animals. Keeping animals physically separated can be challenging; in-contact animals can be bathed with a topical antifungal shampoo (see ***Topical Therapy***, next page) or treated with lime sulfur and watched closely for development of lesions.

Cleaning

Cleaning removes shed-infective material in the environment. Cleaning minimizes false-positive fungal cultures (ie, a culture-positive but lesion-free patient) that complicate determination of mycologic cure and prolong treatment. If cleaning is regularly performed while the patient receives topical therapy, most homes can be decontaminated with 1 or 2 cleanings after cure.[5] Any items that can be mechanically washed can also be decontaminated.[1]

Homes do not need to be aggressively cleaned every day; twice-weekly thorough cleaning of the confinement area is usually sufficient. It is important to mechanically remove gross debris (ie, hairs) on a daily basis. The most efficient method is vacuuming, provided the vacuum has a filter to trap debris and is emptied and cleaned after each use. Removal of debris with disposable dust cloths or wet wipes is adequate between aggressive cleanings.

After removal of gross debris, hard surfaces should be washed with detergent until visibly clean, then rinsed, dried, and sprayed with a disinfectant. Over-the-counter, ready-to-use bathroom disinfectant cleaners with a label claim that it is an antifungal against *Trichophyton* spp or products containing accelerated hydrogen peroxide are effective against dermatophytes.[6] Bleach should be avoided, as it can be an irritant, can damage surfaces, and has no detergent properties.

Exposed textiles and soft items should be washed twice with any common laundry detergent on the longest wash cycle possible. Bleach and/or hot water

DTM = dermatophyte test medium

For more on performing fungal cultures, see **cliniciansbrief.com/article/fungal-cultures**

have not been found to be superior to cold water without bleach.[7] Fabric should be dried according to its label instructions. Agitation from washing (not drying) is antifungal; household dryers do not reach temperatures that are sporicidal. Carpets can be decontaminated by being washed with a beater-brush rug cleaner twice or steam cleaned once. If a disinfectant is desired, antifungal pet shampoo can be substituted for carpet detergent, but color testing should be performed prior to use.[8]

Pet food bowls can be decontaminated via thorough washing with hot, soapy water.[9]

Topical Therapy

Topical treatment of the hair coat is not considered an optional part of therapy. Topical therapy decreases shedding of infective material, kills ectothrix spores (not affected by systemic therapy[1]) on the hair coat, helps prevent development of new lesions, and decreases contagion and environmental contamination. Clipping of the hair coat is not routinely needed, but infected hair may be clipped with metal blunt-tip scissors (ie, to avoid microtrauma to skin from electric clippers). The coat should be combed before application to remove loose hairs. Whole-body hair coat disinfection twice weekly is recommended. Patients should be kept warm (eg, with warm blankets) following whole-body treatment to prevent hypothermia.

In vitro and in vivo studies have shown lime sulfur, miconazole/chlorhexidine gluconate, and enilconazole to be consistently effective.[1] Leave-on rinses are preferred because of their residual activity and should be applied to the face with a sponge.

Topical treatment of the hair coat is not considered an optional part of therapy.

Leave-on lime sulfur rinse should be applied twice weekly at a 1:16 dilution. This product, which is not available in all countries, may discolor the hair coat and is somewhat odorous. It will also stain fabric and discolor items in contact with it; owners must wear gloves when applying the product and should not let it come into contact with watches or jewelry. Owners should be educated about proper dilution, as concentrated application can be irritating to the skin. Lime sulfur is efficacious, is immediately sporicidal, and has residual activity. Lime sulfur can be drying to the hair coat or footpads when used for prolonged periods. In the author's experience in shelters, oral ulcers were never observed as a result of use of lime sulfur; cats with oral ulcers had concurrent respiratory infections.

Miconazole (2%)/chlorhexidine gluconate (2%) shampoo is widely available and is sporicidal but does not have residual activity. Although no in vivo studies have determined the optimal contact time, an in vitro study found that 3 minutes of contact was sporicidal[10]; therefore, 3 to 10 minutes of contact is recommended. This shampoo can also be used for treatment of exposed but uninfected animals in the home.

Enilconazole leave-on emulsion (1:50 or 1:100) is only labeled for use in cats in France and is not available in all countries. The emulsion is slightly odorous and may be greasy.

Adjuvant focal topical therapy applied once daily is recommended for focal lesions and/or lesions in areas that are difficult to treat (eg, face, ears). This is in contrast to recommendations in most veterinary dermatology textbooks that recommend application twice daily. A recent in vitro study demonstrated good residual activity of clotrimazole (1%), terbinafine (1%), miconazole (0.2%, 1%, or 2%), and 3 leave-on mousse products containing chlorhexidine and climbazole, miconazole, or ketoconazole.[10] Mousse products may be suitable for animals that cannot be wetted or are difficult to treat. Care must be taken to use the product as directed by the manufacturer. For periocular lesions, 2% miconazole

nitrate vaginal cream is recommended[11,12]; this product is widely used with proven safety by ophthalmologists to treat fungal keratitis. Lesions on or in the ears are best treated with otic preparations with antifungal efficacy.

Owners should always wear gloves when applying topical therapy.

Systemic Therapy

Systemic therapy eradicates infection in the hair follicle and is considered to be an important and necessary part of therapy. Itraconazole (noncompounded) and terbinafine are the most effective and safe treatments for dermatophytosis and have residual activity in the skin and hair, allowing for pulse therapy. Compounded itraconazole should not be used due to poor bioavailability.[13,14] In cats, itraconazole should be administered at 5 mg/kg PO once daily on a week on/week off basis until mycologic cure (see ***Guidelines for Determining Mycologic Cure***). Because this drug is difficult to get into a suspension, the veterinary or human pediatric liquid suspension should be used. If neither is available, 100-mg capsules can be repackaged into 25-mg capsules.

Experimental and field studies have found this drug to be well tolerated, with the most adverse side effects being vomiting and/or decreased appetite.[1] In a licensing study, elevations of liver enzymes posttreatment were noted but deemed to be of little clinical significance, and most remained within normal laboratory values.[15] In a shelter study, 21 cats with dermatophytosis had serum chemistry profile results monitored pre- and posttreatment (ie, itraconazole at 5 mg/kg PO once daily for 21 days). No cats became ill or anorexic. A statistically significant increase in alanine aminotransferase was noted, but no values were outside normal reference ranges.[16] Based on these findings, routine monitoring of liver enzymes is not routinely needed in otherwise healthy animals. Monitoring serum chemistry profiles is important in animals with comorbidities.

Alternatively, terbinafine (30-40 mg/kg PO once daily) may be administered until mycologic cure. Some cats given terbinafine may experience GI effects. In small dogs, itraconazole at 5 mg/kg PO may be administered once daily. Pulse therapy options (eg, week on/week off) may likely be appropriate for dogs, but this has not been confirmed. In larger dogs, terbinafine at 30-40 mg/kg PO should be administered once daily.

Griseofulvin, which is fungistatic and teratogenic and requires intensive monitoring, is no longer recommended because safer choices exist. Ketoconazole and fluconazole are not recommended because they do not have residual activity in the skin and have higher MIC than do itraconazole and terbinafine.

Monitoring

Infected patients should be treated until mycologic and clinical cure are achieved (see ***Guidelines for Determining Mycologic Cure***). Clinical cure commonly precedes mycologic cure and can occur within weeks of treatment initiation. A recent study showed that when compliance with treatment and environmental cleaning was high, 1 negative fungal

GUIDELINES FOR DETERMINING MYCOLOGIC CURE

- Topical therapy should be continued pending the results of all posttreatment fungal cultures.
- In otherwise healthy animals, the first posttreatment fungal culture should be obtained after the prescribed treatment protocol is completed *and* the patient is lesion free with negative Wood's lamp results for *M canis* infections. If the culture is negative, the patient could be assumed cured.
- In patients that were clinically ill at the time of diagnosis, were unthrifty (eg, not clinically well), or for which there is concern about treatment compliance, the first posttreatment fungal culture should be delayed until there is both clinical cure and resolution of any underlying medical problems or treatment issues. Two consecutive fungal cultures at weekly intervals are recommended to ensure cure.

culture was predictive of mycologic cure.[16] If 2 negative fungal cultures are needed (eg, patient has underlying illness, compliance issues are suspect), they should be obtained at weekly intervals.

Prognosis is good in patients with superficial dermatophytosis and dogs with kerion reactions. Prognosis is less certain in patients with SC nodular lesions; these patients, particularly cats, often require surgical intervention and long-term therapy.

Immunocompromised humans should avoid contact with infected animals during treatment, as is the case in any animal-acquired disease.[17]

Clinical Challenges

Culture-positive, lesion-free cats are typically fomite carriers or have subtle lesions not detected at initial examination and should be carefully reexamined (including the head and between the digits) with a Wood's lamp. Wood's lamp examination may identify lesions or sites of early infection not visible under examination room light. If no lesions are found, the cat should be bathed with an antifungal shampoo or treated with a lime sulfur rinse; the fungal culture should be obtained again when the cat is dry. Topical therapy should be continued until fungal culture results are available. Commonly, these cats rapidly become fungal culture-negative when allowed to groom and moved to a clean area.

A persistent positive fungal culture following clinical cure has 3 common causes: inadequate disinfection of the hair coat, fomite carriage due to insufficient cleaning of the home, and development of new lesions in areas that are difficult to treat due to inadequate hair coat disinfection. In the case of fomite carriage, owners should be instructed to aggressively clean the patient's living area and repeat topical therapy; culture testing should be performed again when the cat is dry or within 24 hours.

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Lymphopenia

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

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

Following are differential diagnoses for patients presented with lymphopenia.

- Acute infection, particularly viral
- Cytotoxic or immunosuppressive drug (eg, chlorambucil, cyclophosphamide)
- Destruction/disruption of lymphoid tissue (eg, multicentric lymphoma)
- Immunodeficiency (rare; eg, severe combined immunodeficiency syndrome in basset hounds, Cardigan Welsh corgis, Jack Russell terriers, Frisian water dogs)
- Increased exposure to endogenous corticosteroids
  - Acute illness
  - Hyperadrenocorticism
  - Stress (eg, surgery)
- Increased exposure to exogenous corticosteroids
  - Steroid therapy
  - Contact with steroid creams in household
- Loss of lymphocytes (eg, into intestinal tract with lymphangiectasia, into pleural cavity with chylothorax)
- Whole body irradiation

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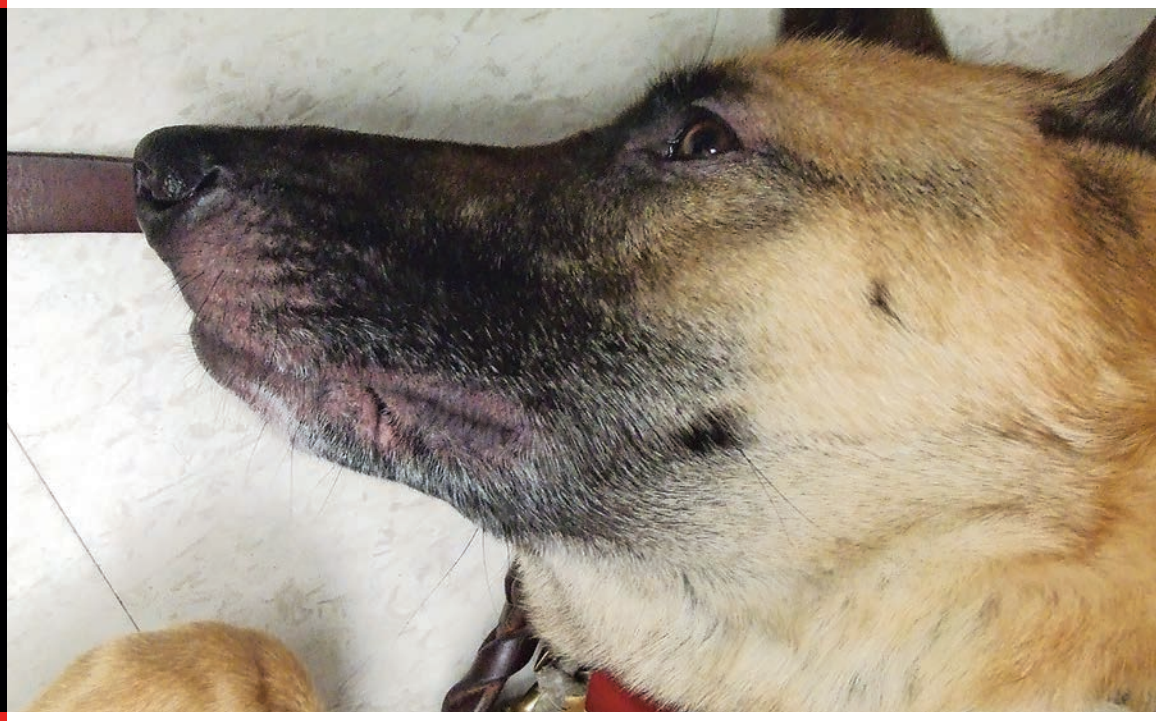
FROM PAGE TO PATIENT

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



RESEARCH NOTES

Effect of Peritoneal Lavage in Dogs with Septic Peritonitis

Katie Hoddinott, BSc, DVM, DVSc, DACVS-SA
University of Prince Edward Island
Prince Edward Island, Canada

In the Literature

Marshall H, Sinnott-Stutzman V, Ewing P, Bracker K, Kalis R, Khorzad R. Effect of peritoneal lavage on bacterial isolates in 40 dogs with confirmed septic peritonitis. *J Vet Emerg Crit Care (San Antonio).* 2019;29(6):635-642.

FROM THE PAGE ...

Septic peritonitis is an infection of the peritoneal cavity and often occurs secondary to a ruptured abdominal viscus. Recommendations for treatment have been extrapolated from human medicine and include prompt antimicrobial intervention, surgical treatment for source control, and peritoneal lavage (200-300 mL/kg) to remove/dilute the infectious organisms.[1-3]

Forty dogs diagnosed with first-time septic peritonitis between 2011 and 2015 were enrolled in this prospective study evaluating bacterial isolate type, susceptibility, and change in resistance between pre- and postlavage samples. Culture samples were collected intraoperatively before and after lavage. Swabs contacted both the body wall and affected viscera during collection. Prelavage samples were collected on entry to the abdomen, and postlavage samples were collected before closure following sterile glove change. All swabs were submitted for aerobic and anaerobic culture testing.

Empiric antimicrobial therapy was instituted in all dogs preoperatively, with 39 out of 40 (97.5%) receiving appropriate antimicrobials based on pre- and postlavage culture results. Prelavage cultures were positive in 37 out of 40 (92.5%) cases, whereas postlavage cultures were positive in 35 out of 40 (87.5%) cases. Forty-six new isolates were identified in 20 out of 40 dogs; however, a decrease in total number of bacterial isolates was noted in postlavage cultures. The most common bacterial isolates included *Escherichia coli, Clostridium perfringens*, and *Enterococcus faecalis.* There was no significant difference in overall resistance between pre- and postlavage

samples, although multidrug resistance was identified less commonly post-lavage. Survival to discharge occurred in 35 out of 40 (87.5%) dogs, including 1 dog that received inappropriate empiric antimicrobial therapy.

Peritoneal lavage has an effect on both the number and type of bacteria isolated in patients with septic peritonitis. In this study, source control and lavage successfully reduced the overall number of bacterial isolates between pre- and postlavage samples. However, new isolates identified postlavage likely represent mobilization of bacteria during lavage that were not accessible at the time of prelavage sampling. The reduction in multidrug-resistant isolates between pre- and postlavage samples is attributed to source control and lavage, as these were the only interventions performed between sample collections. Early empiric antimicrobial therapy must be initiated for all cases of septic peritonitis; however, critical use of culture results for rapid de-escalation of antimicrobial therapy is paramount. Overall survival (87.5%) to discharge for septic peritonitis was higher than previously reported.

… TO YOUR PATIENTS

Key pearls to put into practice:

1. Clinicians should continue to follow previous recommendations for septic peritonitis, including prompt antimicrobial intervention, surgical treatment for source control, and peritoneal lavage.
2. When collecting culture swabs, clinicians should ensure swabs contact not only the abdominal fluid but also the body wall and affected viscera.
3. To guide appropriate de-escalation of antimicrobial therapy, clinicians should consider collecting both pre- and postlavage samples to ensure all bacterial isolates are identified. If the pet owner has financial constraints, pooling pre- and postlavage samples can be considered to reduce cost while not compromising the identification of bacterial isolates.

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See page 48 for product information summary.

Simplifying Dietary Elimination Trials

Alison Diesel, DVM, DACVD
Texas A&M University

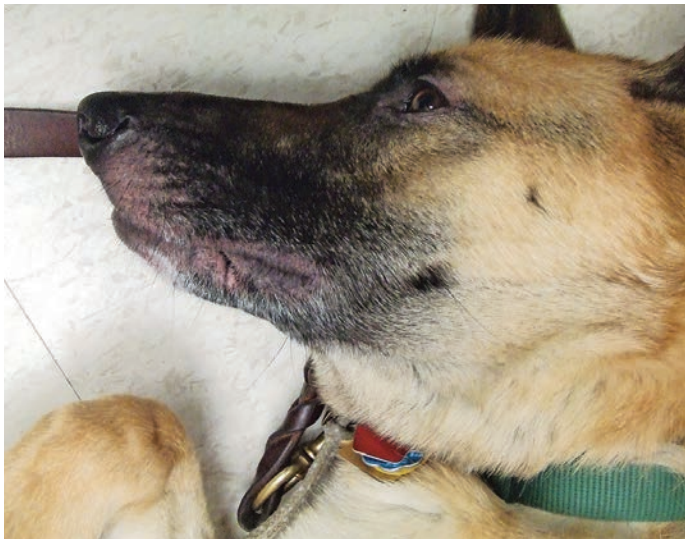
In the literature

Favrot C, Bizikova P, Fischer N, Rostaher A, Olivry T. The usefulness of short-course prednisolone during the initial phase of an elimination diet trial in dogs with food-induced atopic dermatitis. *Vet Dermatol*. 2019;30(6):498-e149.

FROM THE PAGE ...

Although less common than atopic dermatitis caused by environmental allergens, cutaneous adverse food reaction (ie, food allergy, food-induced atopic dermatitis) is an important differential diagnosis in a pruritic dog when infections, including parasitic infections, have been ruled out. Diagnosis is typically based on the results of an 8- to 12-week dietary elimination trial, which can often be difficult to perform due to a lack of appropriate pet owner compliance.

The aim of this prospective study* was to evaluate the usefulness of administering a short course of oral prednisolone for a minimum of 2 weeks of a dietary elimination trial to reduce the time required to confirm or refute a food allergy diagnosis. Fifty-three dogs with a diagnosis of nonseasonal atopic dermatitis were fed a commercially available, extensively hydrolyzed diet and given anti-inflammatory dosages of prednisolone for ≥2 weeks. Two weeks after prednisolone was discontinued, 10 of the 53 dogs did not show signs of flare-up; these dogs were then challenged with their original diets and experienced relapse of signs. When the extensively hydrolyzed



▲ **FIGURE** German shepherd dog with cutaneous adverse food reaction. This dog had concurrent environmental allergy. Both food and environmental triggers exacerbate clinical signs of atopic dermatitis.

diet was reintroduced to this group, clinical signs improved. These dogs were subsequently diagnosed with food-induced atopic dermatitis. Median duration of the food elimination trial for the food-allergic dogs was 28 days (range, 28-44 days). In the other 43 dogs, pruritus could not be controlled without concurrent prednisolone administration and clinical signs did not worsen with diet challenge. In these dogs, elimination diet trials lasted a median of 60 days (range, 54-70 days).

… TO YOUR PATIENTS

Key pearls to put into practice:

1 Historically, atopic dermatitis has been referred to as allergic skin disease triggered by environmental allergens. There is growing evidence that supports food as a possible trigger for some dogs with atopic dermatitis.[1] In these dogs, pruritic skin disease with clinical characteristics of atopic dermatitis can develop with ingestion of various foods. Canine food allergy is believed to involve both immunologic and nonimmunologic pathomechanisms of development[2]; this could support shared immunologic responses in the conditions previously considered to be separate.

2 A strict dietary elimination trial remains the gold standard for diagnosing food allergy in dogs and cats. A recent literature review evaluated information on in vitro and in vivo testing for food allergies in veterinary species[3]; results lack support for any evaluated test other than diet trial. However, these trials can be frustrating for owners and often lead to noncompliance. Concurrent administration of anti-inflammatory steroids as described in the present study may allow for reduced time to achieve a diagnosis in truly food-allergic dogs.

3 Reducing inflammation is key when managing allergic skin disease in dogs and cats. Focusing on this in the early stages of dietary elimination trials can help dampen pathways that lead to itch and inflammation. Steroids have a broad effect with regard to inflammation; whether these same effects would be noted with more targeted therapeutics (eg, oclacitinib, lokivetmab) is unknown.

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*Royal Canin provided free food and contributed to additional costs associated with study follow-up.

See page 48 for product information summary.

NexGard®
(afoxolaner) Chewables

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

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

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

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

Dosing Schedule:

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

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

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

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

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

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

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

Keep NexGard in a secure location out of reach of dogs, cats, and other animals to prevent accidental ingestion or overdose.

Precautions:
Afoxolaner is a member of the isoxazoline class. This class has been associated with neurologic adverse reactions including tremors, ataxia, and seizures. Seizures have been reported in dogs receiving isoxazoline class drugs, even in dogs without a history of seizures. Use with caution in dogs with a history of seizures or neurologic disorders.

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

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

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

Table 1: Dogs With Adverse Reactions.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Approved by FDA under NADA # 141-406

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Research Note:
Temporal Changes in Dogs with Preclinical Myxomatous Mitral Valve Disease

In this study, the authors describe the temporal changes in clinical and radiographic variables prior to development of congestive heart failure (CHF) in dogs with stage B2 myxomatous mitral valve disease. Dogs developing CHF showed increased heart rates, respiratory rates at home and in the clinic, and vertebral heart sums. Rectal temperatures and body weights were decreased. Vertebral heart sums gradually increased over 12 months, whereas the other variables changed in the 2 to 10 months prior to developing CHF. The variables with the highest absolute change and rate of change were observed with respiratory rates at home and in the clinic, suggesting monitoring of these variables may enable earlier detection and management of CHF.

Source

Boswood A, Gordon SG, Häggström J, et al. Temporal changes in clinical and radiographic variables in dogs with preclinical myxomatous mitral valve disease: the EPIC study. *J Vet Intern Med*. 2020;34(3):1108-1118.

Research Note:
Novel Serologic Markers & Autoantibodies in Dogs with Inflammatory Bowel Disease

The prevalence of inflammatory bowel disease (IBD) in dogs warrants an easier route for diagnosis, as the current path is costly, invasive, and time-consuming. In this study, researchers explored the possibility of using serologic markers for diagnosis of IBD in dogs, similar to what is done in human medicine. Serologic markers represent the patient's reaction to translocation of GI pathogens in the bloodstream when the gut mucosal barrier breaks down. Three cohorts were studied: dogs diagnosed with IBD via biopsy, dogs with acute GI signs from causes other than IBD, and a normal cohort. ELISA methods were developed to detect autoantibodies against canine polymorphonuclear leukocytes (ie, antipolymorphonuclear leukocytes antibody [APMNA]) and calprotectin, microbial outer membrane porin C (OmpC), antibodies against food-derived gliadins, and flagellins isolated from diseased dogs. Of these, antibodies against APMNA and *Escherichia coli* OmpC exhibited the highest single-marker performance for discriminating IBD from other acute GI conditions and normal cohorts.

Source

Estruch JJ, Barken D, Bennett N, et al. Evaluation of novel serological markers and autoantibodies in dogs with inflammatory bowel disease. *J Vet Intern Med*. 2020;34(3):1177-1186.

See page 48 for product information summary.

Parasite Prevalence in Feline Feces

Nancy Vincent-Johnson, DVM, MS, DACVIM (SAIM), DACVPM
Fort Belvoir Veterinary Center
Fort Belvoir, Virginia

In the Literature

Nagamori Y, Payton ME, Looper E, Apple H, Johnson EM. Retrospective survey of parasitism identified in feces of client-owned cats in North America from 2007 through 2018. *Vet Parasitol*. 2020;277:109008.

FROM THE PAGE ...

Feline parasitism not only has the potential to produce disease and unthriftiness in cats but can also cause zoonotic disease in humans (eg, ocular or visceral larval migrans, toxoplasmosis). Therefore, identifying the prevalence and types of parasites seen in cats can be beneficial.

The objective of this retrospective study was to comprehensively evaluate the prevalence and trend of parasitism in client-owned cats over a 12-year period. Results of fecal examinations performed at 2 locations between 2007 and 2018 were evaluated. Results came primarily from the examination of centrifugal flotation with either Sheather's sugar or zinc sulfate solutions but also included saline direct smears, sedimentation, and Baermann tests. Of the 2,586 samples tested, parasites were observed in 24.5% of samples, with multiple parasites identified in 5.7% of samples. Twenty-three different types of parasites were identified, with the most common being *Cystoisospora* spp (9.4%), *Toxocara cati* (7.8%), *Giardia* spp (4%), *Alaria* spp (3.5%), *Ancyclostoma* spp (1.2%), taeniid (1.2%), *Dipylidium caninum* (1.1%), and *Eucoleus* (syn *Capillaria*) *aerophilus* (0.7%). A significant difference in prevalence was identified between age categories, with the youngest group (<6 months of age) having the highest infection rate (ie, 41%). Prevalence of parasites decreased in each subsequent older age group. The prevalence of *Cystoisospora* spp and *T cati* increased in summer months through fall; this seasonality is likely due to the litters of kittens born in spring and summer. The prevalence rate of parasitism increased over the 12-year period.

… TO YOUR PATIENTS

Key pearls to put into practice:

1 Although fecal flotation is the most common method of parasitism testing, it is not always the best technique for all parasites. Heavy trematode eggs do not reliably float and are better identified through fecal sedimentation. The Baermann technique is the best test for identifying lungworm larvae. Fecal flotation techniques also differ in their ability to reveal various ova and protozoa[1]; the specific gravity of the solution affects the variety of ova and protozoa that float and can also cause distortion, making them harder to detect, and centrifugal flotation is more sensitive than passive flotation.[2] The type of test should be selected based on the patient's history and expected findings.

2 Review of medical records in this study revealed that all cats positive for the rare parasites *Trichuris felis* and *Platynosomum fastosum* had recently moved from the Caribbean. When animals are imported from outside the United States or travel with their owners, they may transport exotic diseases. Therefore, clinicians should be familiar with nonendemic parasites to avoid overlooking or misdiagnosing them.

3 This study showed that the prevalence rate of feline parasitism continued to increase over the 12-year study period. Along with owner education and year-round, broad-spectrum parasite control, it is vital that clinicians continue to conduct parasite testing and treatment, especially in kittens and young cats.

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Suggested Reading

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Antimicrobial Resistance in Canine Urinary Tract Infections

India Lane, DVM, MS, EdD
University of Tennessee

In the Literature

Yu Z, Wang Y, Chen Y, et al. Antimicrobial resistance of bacterial pathogens isolated from canine urinary tract infections. *Vet Microbiol*. 2020;241:108540.

FROM THE PAGE ...

Although UTIs are relatively common in female dogs and other reviews have been published, the authors of this study from Beijing, China, recognized a possibility for variance in the local and regional population. To further understand the prevalence and antimicrobial resistance of bacteria associated with canine UTIs, analysis of urine samples from dogs with UTIs or other urinary tract diseases was performed.

In processing 326 samples, 129 bacterial isolates were identified from 103 samples. The isolated organisms were similar to other reports[1]; *Escherichia coli* was identified most commonly but only represented approximately one-third of total positive cultures. A variety of other gram-positive and gram-negative organisms comprised the remaining isolates, with *E coli, Klebsiella* spp, and *Staphylococcus* spp comprising ≈70% of positive cultures. More than one pathogen was isolated in ≈33% of positive cases. Resistance to common antimicrobials was also common in positive samples. In *E coli* isolates, the highest rates of resistance were recorded for ampicillin, ceftazidime, and florfenicol. The highest rates of resistance in *Staphylococcus* spp isolates were recorded for erythromycin, trimethoprim/sulfamethoxazole, and penicillin. These results reinforce the importance of culture and antimicrobial susceptibility testing when planning appropriate UTI treatment.

The results of this study suggest the existence of rampant multidrug-resistant urinary tract pathogens in the region in which the study took place; however, they are also fairly consistent with what is seen in typical small animal practice.[1] Even with expert screening of urine sediment, only ≈33% of urine cultures grew organisms; negative urine cultures may represent prior antimicrobial treatment, true negatives, or misidentification of sediment artifacts. However, samples from dogs with signs of UTI but unremarkable sediments were not cultured; thus, other infected dogs may have been missed. In addition, although *E coli* may be expected to cause a proportion of UTIs, two-thirds of cases are caused by other bacteria, and a significant variance in antimicrobial susceptibility can be expected.

… TO YOUR PATIENTS

Key pearls to put into practice:

1. This study provides a glimpse of the value of antibiograms and the need for antimicrobial stewardship. An antibiogram assimilates the susceptibility patterns from large numbers of samples at a single laboratory, region, or hospital. Antibiograms are particularly pertinent for hospital-acquired infections, both for planning treatment and tracking resistance patterns. Although an antibiogram does not replace individual susceptibility testing in the management of infection, it does provide some generalizable information to guide empiric treatment selection.

2. Nearly all urinary pathogens in this study remained susceptible to amikacin and meropenem; however, cost, toxicity, and practicality of these medications limit their clinical value. Similarly, doxycycline appears promising based solely on the antibiogram in this study, but it is not excreted at high levels in urine and is usually reserved for infections resistant to other treatment options.

3. Antimicrobial stewardship entails limiting antimicrobial exposure and reducing the risk for resistant organisms. Consensus guidelines are available for shorter, targeted, and selective management of UTIs in dogs and cats[2]; although these guidelines rely heavily on human medical literature and practice and are yet to be tested in veterinary practice, they provide a conservative view of antimicrobial treatment worth adopting. By prioritizing stewardship, reasonable empiric antimicrobial choices, and short treatments based on culture and susceptibility results, the veterinary profession can help support good patient care while blunting induced resistance.

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Intrahousehold Interdog Aggression

Bonnie V. Beaver, DVM, MS, DSc (Hon), DPNAP, DACVB, DACAW
Texas A&M University

In the Literature

Feltes ESM, Stull JW, Herron ME, Haug LI. Characteristics of intrahousehold interdog aggression and dog and pair factors associated with a poor outcome. *J Am Vet Med Assoc*. 2020;256(3):349-361.

FROM THE PAGE ...

Interdog aggression in a home can be disturbing and frustrating to pet owners, disruptive to everyday life, and potentially dangerous to both the owner and the dogs. The more that can be understood about this problem, the better advice a clinician can give the owner.

This review presented the results of a large, well-designed study that evaluated 305 pairs of dogs (217 included in outcome analysis) presented to a behavior referral practice for aggression toward each other. Cases reviewed had ≥6 months of follow-up or ≥1 of the dogs euthanized or permanently removed from the home. Multiple factors were assessed to determine correlations between interdog aggression and long-term outcome. Many of the results also support previous studies.[1,2]

Intrahousehold interdog aggression is typically associated with dog pairs in which resource guarding is a trigger, a fighting pair of dogs that includes ≥1 female dog,[1] dogs of the same sex,[1] situations in which the aggressor dog was acquired after the recipient dog and is younger,[2] and aggressor dogs that are purebred but not breed-specific.[1,2] Several of these correlations were seen in ≥50% of the cases.

For the 217 pairs that were followed long-term, 55 pairs (25.3%) had poor outcomes, which included 23 pairs that required complete separation from one another, 24 involving ≥1 dog being euthanized, and 8 involving ≥1 dog being rehomed.[2] Of the remaining 162 pairs with a better outcome, 100 (61.7%) did not have to be separated following behavioral intervention, 32 (19.8%) were separated during triggers, 21 (13%) were kept separate when unsupervised and during triggers, and 9 (5.6%) were kept muzzled when together and supervised.[2]

… TO YOUR PATIENTS

Key pearls to put into practice:

1 Risk factors significantly associated with a poor outcome (eg, euthanasia, permanent separation of the dogs) in dogs with interdog aggression include[1,2]:

- Dogs of the same sex, particularly female–female
- A bite serious enough to puncture the skin of the recipient
- The aggressor is ≥2 years younger than the recipient.
- The aggressor was introduced into the household after the recipient.
- An aggressor that is heavier than the recipient
- The aggression is triggered by the sight of the recipient, even without other triggers.
- The owner uses positive-punishment/negative-reinforcement training techniques.

2 Management is a particularly important part of treatment and should be strongly encouraged when clinicians become aware of the problem. Triggers should be removed if possible. The dogs should be kept separate from each other—particularly if eye contact alone triggers the aggression, when triggers are present, and when unsupervised. Muzzles are recommended, and appropriate muzzle training is emphasized. A variety of psychopharmacologic medications may be helpful. In this study, such medications were prescribed for 82.4% of aggressors and 32.7% of recipient dogs.

3 Ultimately, when historical information points to risk factors associated with poor outcomes (as described above), strong and immediate intervention is called for by the clinician, often including referral to a board-certified veterinary behaviorist.

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Tail-Pull Injuries in Cats

Jonathan Miller, DVM, MS, DACVS
Oradell Animal Hospital
Paramus, New Jersey

In the Literature

Couper E, De Decker S. Evaluation of prognostic factors for return of urinary and defecatory function in cats with sacrocaudal luxation. *J Feline Med Surg*. 2020. doi: 10.1177/1098612X19895053

FROM THE PAGE ...

Sacrocaudal luxations (ie, tail-pull injuries) are relatively common in cats and present as a limp, sometimes painful, tail. Assessing nerve function is important during physical examination of patients presented with this condition; testing should be performed for distal and proximal tail sensation, anal tone, and perineal reflex. Damage to the caudal nerves can cause decreased sensory and motor function to the tail, and damage to the pelvic and pudendal nerves affects urine and fecal continence.

The goal of this study was to assess long-term outcome and prognostic factors in cats with sacrocaudal luxation. Seventy cats were evaluated retrospectively; 60 had absent tail tone and 53 had absent tail-base sensation. Anal tone was absent in 20 cats and decreased in an additional 13 cats. Inability to urinate voluntarily was noted in 53 cats; inability to defecate voluntarily was observed in 29 cats. Twenty-one of the cats with an inability to defecate voluntarily were constipated, whereas 8 were fecally incontinent.

Of the 61 cats for which urinary outcomes were available, 90% regained voluntary urinary function; 87% of those regained it in <30 days. Cats with a flaccid incontinent urinary bladder had a significantly worse prognosis, with only 50% regaining urinary control at a median of 33 days. With regard to fecal continence, 25% of those incontinent at presentation remained so, and 68.4% of those experiencing constipation at the time of injury continued to experience it at the time of follow-up. Age, sex, tail-base sensation, anal tone, perineal sensation, fecal continence, degree of vertebral displacement, and tail amputation did not affect outcome. Despite nerve dysfunction commonly being noted at the time of injury, most cats regained function with time. Because early tail amputation did not affect outcome, the authors did not recommend this as a treatment for cats with sacrocaudal luxation.

... TO YOUR PATIENTS

Key pearls to put into practice:

1. Cats with sacrocaudal luxation should undergo a thorough neurologic examination, including careful evaluation of bladder and anal tone.
2. Overall, cats with sacrocaudal luxation have a good prognosis for return to function; urinary incontinence with a flaccid bladder may be associated with a worse prognosis.
3. Based on the high percentage of cats that returned to function in this study, aggressive decisions about euthanasia or tail amputation should not be made until at least 6 weeks postinjury.

Research Note:
MRI for Spinal Cord & Soft Tissue Injury Evaluation

Although CT is considered the gold standard for detecting vertebral fractures, human studies have suggested that MRI may be used as a single modality to evaluate spinal cord and soft tissue injuries in addition to vertebral fractures. In this study of 128 vertebrae in 33 dogs, only moderate agreement between 2 expert observers was achieved when evaluating vertebral fractures using MRI, although agreement was substantial with structurally unstable fractures. Fractures in the transverse process were particularly more likely to be missed. It was concluded that MRI is a poor modality for assessing fracture morphology and that, although MRI may be useful for detecting unstable fractures, it should not replace CT for complete evaluation when this modality is available.

Source

Gallastagui A, Davies E, Zwingenberger AL, Nykamp S, Rishniw M, Johnson PJ. MRI has limited agreement with CT in the evaluation of vertebral fractures of the canine trauma patient. *Vet Radiol Ultrasound*. 2019;60(5):533-542.


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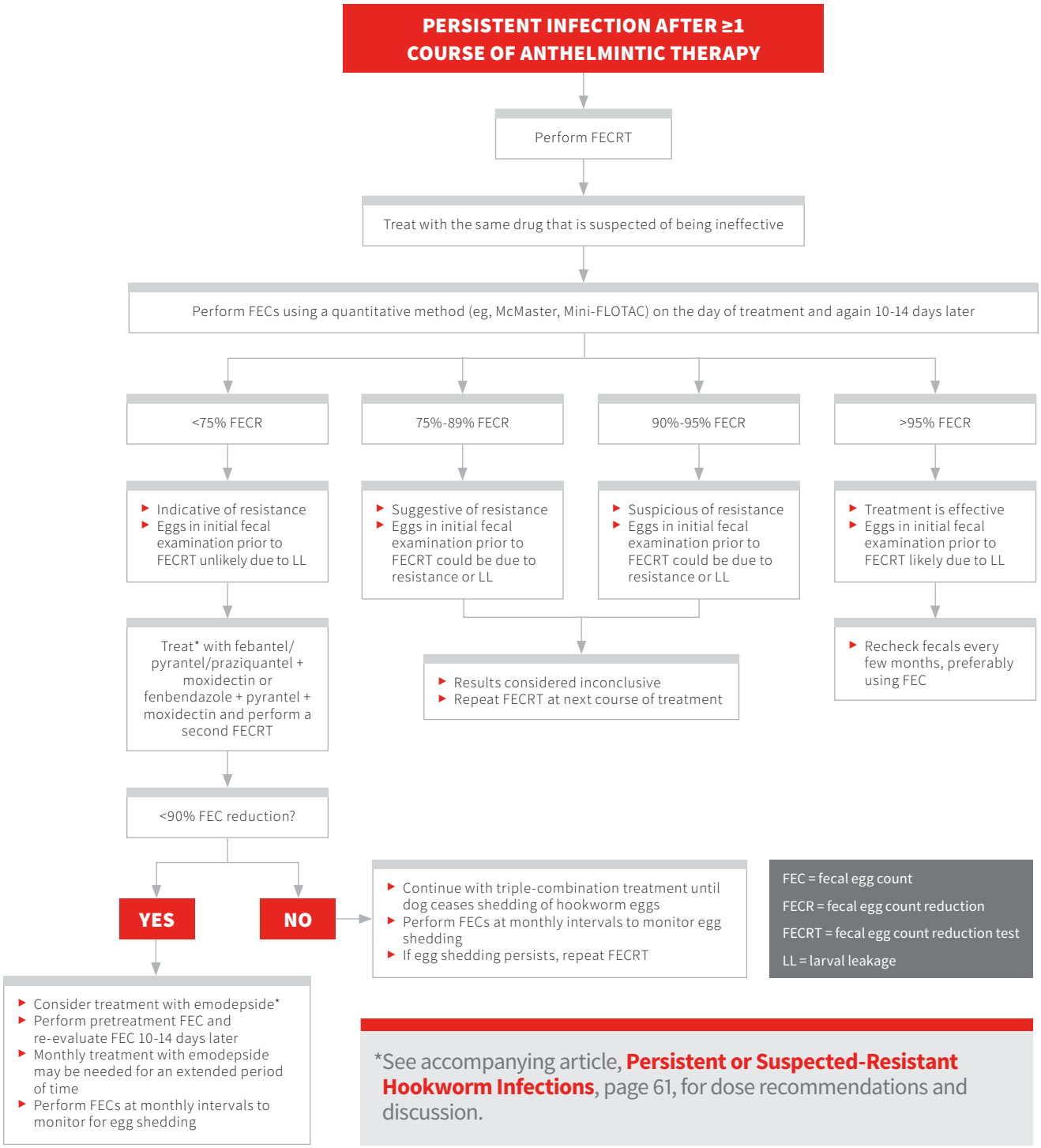
PERSISTENT HOOKWORM INFECTIONS IN DOGS

Pablo David Jimenez Castro, DVM
Ray M. Kaplan, DVM, PhD, DEVPC, DACVM (Parasitology)
University of Georgia



*See accompanying article, **Persistent or Suspected-Resistant Hookworm Infections**, page 61, for dose recommendations and discussion.

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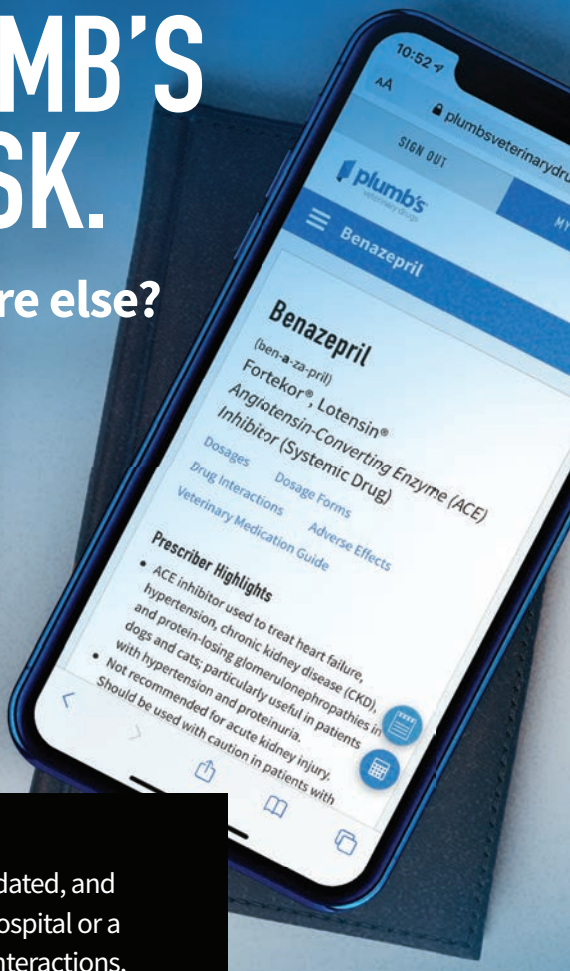

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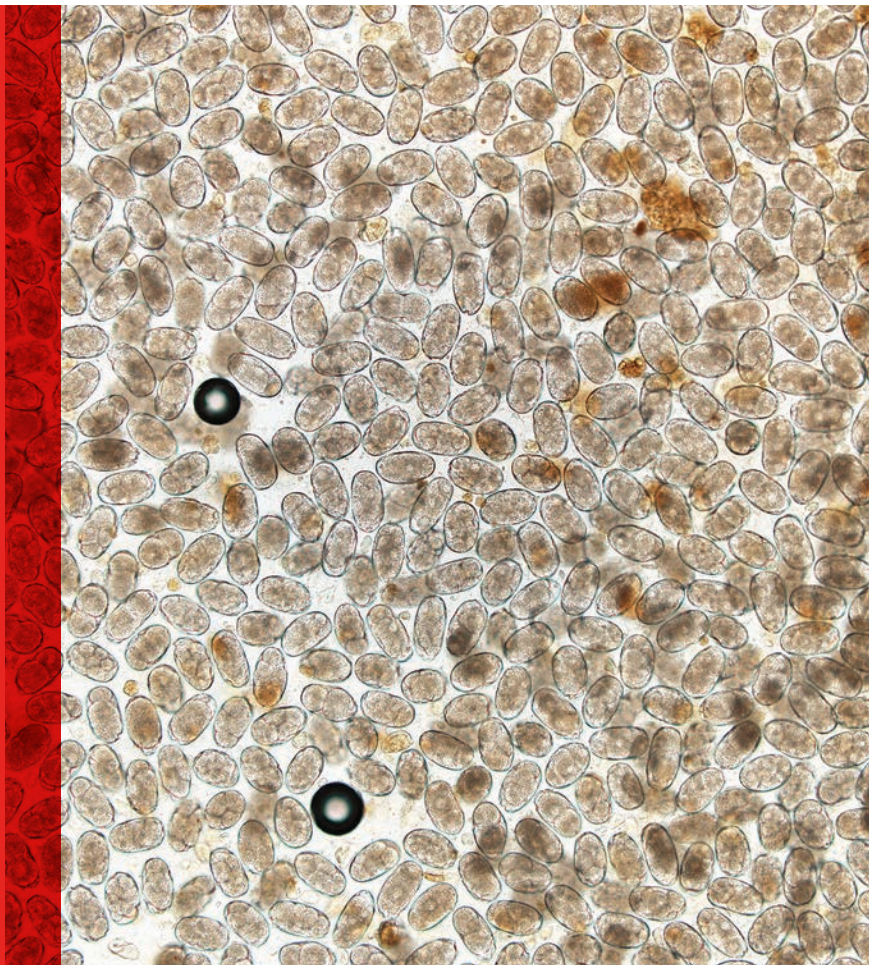
Persistent or Suspected-Resistant Hookworm Infections



Pablo David Jimenez Castro, DVM
Ray M. Kaplan, DVM, PhD, DEVPC, DACVM (Parasitology)
University of Georgia

Numerous cases of canine hookworm (ie, *Ancylostoma caninum*) with multidrug resistance to all 3 major anthelmintic classes have been identified.[1]

Background & Pathophysiology

Diagnostic surveillance performed at the authors' laboratory over the past few years suggests the presence of multidrug-resistant (MDR) hookworms (ie, *A caninum*) likely evolved on greyhound breeding farms and in racing kennels. Most, if not all, actively racing and/or recently adopted greyhounds appear to be infected with MDR hookworms; however, many cases of MDR hookworms have been diagnosed in non-greyhound breeds, suggesting MDR hookworms are spreading to the general canine population.

Hookworms (***Figure 1***, next page) have a direct life cycle, with adult females releasing a large number of eggs (up to 10,000/day). Once passed in the feces, development of eggs to third-stage infective larvae (L3) typically takes ≈5 days, although this will vary depending on temperature. Dogs may be infected via both the oral and percutaneous routes. L3 larvae are ingested either directly or by ingestion of paratenic hosts carrying L3 tissue larvae. After penetrating the skin, L3 larvae migrate via the bloodstream to the lungs, penetrate the alveoli, migrate up the bronchial tree to the trachea, are expectorated via coughing, are swallowed, and enter the small intestine, where they complete development into the adult stage. The prepatent period

L3 = third-stage infective larvae
MDR = multidrug-resistant

for either route of infection is 15 to 26 days. Following skin penetration in dogs older than 3 months of age, *A caninum* L3 larvae often undergo somatic migration to the muscle, fat, and other organs; encyst; and enter a hypobiotic state.

Encysted somatic larvae may become reactivated under 2 conditions: host pregnancy or larval leakage (ie, when arrested somatic larvae continuously leak from tissue and complete migration to the intestine, where they develop into adults and begin a new round of egg shedding). An important mode of *A caninum* transmission is the transmammary route, in which puppies become infected by reactivated larvae that migrate to the mammary tissue of the dam.

▲ **FIGURE 1** Anterior end of adult *A caninum*. The buccal capsule (ie, mouth) contains the characteristic 3 pairs of teeth.

EPG = eggs per gram
FEC = fecal egg count
FECRT = fecal egg count reduction test
L3 = third-stage infective larvae
MDR = multidrug-resistant

Although direct evidence is lacking, based on the authors' observations and previous research on this issue in the sheep parasite, *Haemonchus contortus*,[2] it is probable that macrocyclic-lactone resistance has worsened as the use of moxidectin has become more common. Further, drug resistance in nematodes is typically a slow evolutionary process, requiring many years of drug selection to reach levels that are clinically apparent.[3] This was most likely the case for *A caninum*; thus, the level of resistance seen in any particular case and to any particular drug will depend in part on the time frame of the animal's adoption and previous anthelmintic treatments.

The emergence and spread of MDR hookworms that are poorly responsive to typical anthelmintic treatments necessitate a different management approach.

Diagnosis

When addressing persistent cases of *A caninum* infection, the clinician should first differentiate between larval leakage[4] with drug-susceptible *A caninum* and infection with MDR hookworms.

There are 3 methods to diagnose anthelmintic resistance: performing a fecal egg count reduction test (FECRT), submitting a sample to a laboratory that can perform in vitro drug bioassays with hookworms, and submitting a sample to a laboratory that can perform molecular testing for resistance.

FECRT is the ideal practical approach, as laboratory expertise and facilities may not be readily available for the other diagnostic methods. FECRT can be easily accomplished at the clinic level for minimal cost.

Performing a Fecal Egg Count Reduction Test

To perform an FECRT, the number of eggs per gram of feces must be quantified pre- and post-treatment. Fecal flotations, which are frequently performed in small animal practice, are inadequate for an FECRT. The pretreatment fecal sample can be collected either the day before or the day of treatment and should be kept refrigerated until submission to the laboratory to prevent development and hatching of eggs prior to testing.

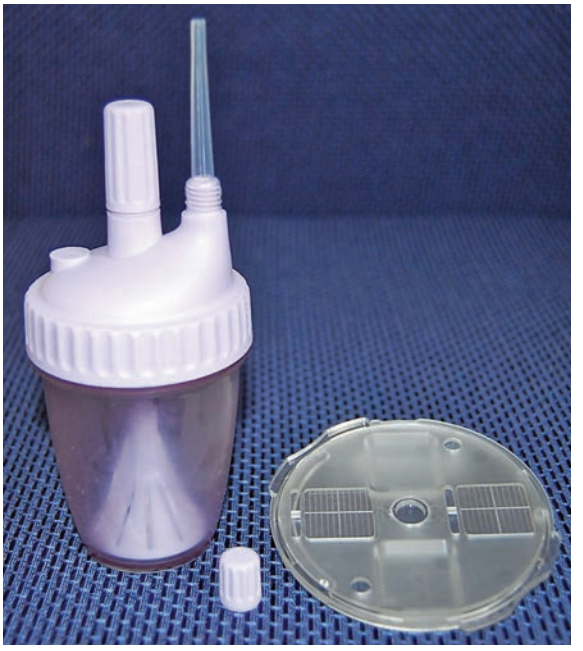
To evaluate for resistance, a quantitative fecal egg count (FEC) method (eg, McMaster,[5] Mini-FLOTAC[6]; ***Figures 2*** and ***3***) is needed. A double-centrifugation method (eg, modified Wisconsin [***Figure 4***]) could also be used but is more time consuming, more labor intensive, less accurate, and less precise.[7,8] A quantitative method is necessary to assess response to treatment. This approach is standard for diagnosis of anthelmintic resistance in livestock nematode parasites, for which drug resistance has been a long-standing problem. Further, because only 1 dog is typically being tested, as compared with groups of 10 to 20 livestock, the authors also recommend performing 2 separate FECs on the pretreatment sample and 2 separate FECs on the posttreatment sample. The FEC reduction is then calculated by comparing the average eggs per gram (EPG) for the 2 pretreatment FECs and the average EPG for the 2 posttreatment FECs. By repeating the FEC, the variability of each FEC measurement will be reduced by half, thus improving the accuracy of the measured FEC reduction.

A specialized laboratory that offers the service should be contacted if in-clinic or diagnostic laboratory FEC testing is not an option. McMaster slides, Mini-FLOTAC reading discs, and Fill-FLOTAC devices are available for purchase (see ***Fecal Egg Count Reduction Test Resources***, next page).

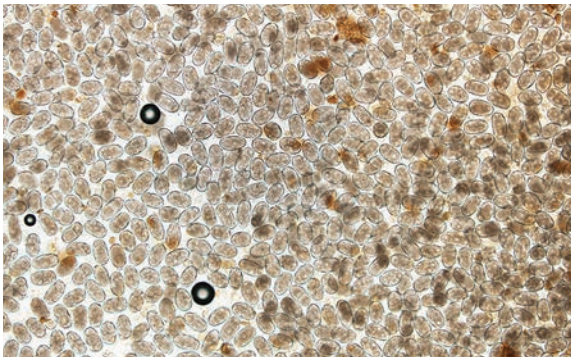
Posttreatment Fecal Egg Count

During testing, the most-recently used anthelmintic should be readministered, even if it elicited poor therapeutic results. Use of an alternate drug will not allow differentiation between larval leakage and

▲ **FIGURE 2** McMaster slide



▲ **FIGURE 3** Fill-FLOTAC and Mini-FLOTAC apparatus. *Image courtesy of Dr. Laura Rinaldi, University of Naples*



▲ **FIGURE 4** Approximately 53,000 EPG (modified Wisconsin) demonstrated in a greyhound puppy that had previously received treatment with several different anthelmintics. *Image courtesy of Dr. Michael Dryden, Kansas State University*

resistance as the cause of treatment failure, as the worms may not be resistant to the new drug. However, this may only be a theoretical concern, as the authors' experience indicates that drug-resistant hookworm infrapopulations most likely will be MDR to all 3 anthelmintic classes.

Multiple days (≥3) are needed for eggs already shed in the intestine to be fully cleared.[9] In addition, the authors have observed a temporary, but high, level of suppression on worm fecundity following fenbendazole treatment. A 99% reduction in FEC has been observed by 3 days posttreatment, with egg counts rapidly rising again after ≈10 days.[1,10] This phenomenon has been reported rarely in sheep after treatment with benzimidazole anthelmintics[11] and on multiple occasions in strongylids of ruminants[12-14] and pigs[15] following treatment with ivermectin and moxidectin. Consequently, checking FEC too soon posttreatment can yield a false-negative result for resistance.

FECAL EGG COUNT REDUCTION TEST RESOURCES

McMaster Slides

- **vetslides.com**
- **eggzamin.com**
- **fecsource.com**
- **hausserscientific.com**

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In contrast, if too much time passes, larvae arrested in somatic tissue could repopulate the intestine and begin a new round of egg shedding, leading to a false-positive result. The prepatent period for *A caninum* has been reported to be as early as 14 days,[16-18] but this time frame is from studies in immune-naive puppies following primary infection. Few data exist on time to worm maturity and egg production in older dogs with chronic infections; however, based on clinical data and other reports,[19] new worms take 3 to 4 weeks to repopulate the lumen of the small intestine and initiate a new round of egg shedding.

The following timeframes are thus recommended for posttreatment FEC: 10 to 14 days after treatment with pyrantel, 14 days after treatment with fenbendazole/febantel, and 14 days after treatment with moxidectin.

The following formula can be used to calculate FECRT percentage:

$$\left(\frac{\text{(Average of pretreatment FEC)} - \text{(Average of posttreatment FEC)}}{\text{Average of pretreatment FEC}}\right) \times 100$$

Interpretation of Fecal Egg Count Reduction Test Results

FECRT results should be interpreted conservatively, as FEC can be highly variable. It is important to note, however, that when commonly used anthelmintics were first approved, high efficacies were reported based on worm counts (>99% for febantel, moxidectin, and milbemycin oxime[20-22]; >98% for fenbendazole[23]; variable for pyrantel, with a mean across studies of ≈94% and over half of studies yielding >99%[24]).

In contrast, in a recent study using an MDR *A caninum* isolate (Worthy 4.1F3P), the efficacies based on worm counts were 23%, 9%, and 26% for pyrantel, milbemycin oxime, and fenbendazole, respectively.[10] The corresponding FEC reductions measured 10 days posttreatment for these same treatments were 13%, 0%, and 46%,

respectively.[10] These data demonstrate that poor FEC reduction can be expected against an MDR *A caninum* isolate following treatment with typical commercial products.

The following interpretation of FEC reduction results are suggested:

- <75% reduction: indicative of resistance (larval leakage is highly unlikely to be the cause of persistent egg shedding)
- 75% to 89% reduction: suggestive of resistance (larval leakage is unlikely to be the cause of persistent egg shedding)
- 90% to 95% reduction: suggestive of reduced efficacy and should raise suspicion for resistance, but results should be viewed as inconclusive (persistent egg shedding could be due to resistance or larval leakage)
- >95% reduction: suggestive of effective treatment (larval leakage is likely the cause of persistent egg shedding)

FECRT is sensitive for detecting resistance (ie, dead worms do not shed eggs); consequently, effective treatment will produce a high reduction in the number of eggs shed, and a poorly effective treatment will yield a low reduction in eggs shed. However, egg-shedding levels on a per-worm basis can vary greatly, and egg production per worm can increase following treatment that kills some of the worms (referred to as *density dependent fecundity*).[25] Therefore, the actual percentage for reduction should not be overinterpreted; for example, 25% and 70% reduction both indicate resistance, but the results should not be interpreted as being greatly different. Likewise, given the expected variability, it should not be assumed that the reduction in FEC will be the same in each case of resistance or even in the same dog if the FECRT is repeated.

FEC reduction between 75% and 95% yields an inconclusive result; repeating FECRT at the next treatment is advised.

Definitive Diagnosis

A diagnosis of resistance should only be established if all of the following are true:

- The patient was treated with the proper dosage.
- The drug administered was within the expiration date and stored properly.
- Fecal samples were labeled and stored correctly prior to fecal analysis.
- An FECRT was performed.
- Proper laboratory techniques were applied when conducting the FECRT, and the same method was used on both the pre- and posttreatment samples.

Treatment & Follow-Up

The treatment plan should depend on the results of the FECRT. If FEC reduction is >95%, treatment should be considered effective. Drugs are not 100% effective, even against drug-susceptible worms; thus, some eggs may be seen, particularly when pretreatment FEC is high. Because resistance can be ruled out, eggs seen on previous fecal examinations are most likely a result of larval leakage. The patient should be treated with an anthelmintic monthly, and fecal examinations should be conducted every few months. Moxidectin can be a good choice in dogs with larval leakage, although any effective anthelmintic should work.

If FEC reduction is between 90% and 95%, FECRT should be repeated a few weeks later at the next treatment.

If FEC reduction is between 75% and 90%, FECRT can be repeated for more conclusive results, or because there is a high chance the worms are resistant, the treatment plan suggested below can be followed.

Continues ▶

FEC = fecal egg count
FECRT = fecal egg count reduction test
MDR = multidrug-resistant

CONSIDERATIONS FOR EXTRA-LABEL EMODEPSIDE

- Due to limited available data, the authors do not recommend extra-label emodepside treatment; however, clinicians can use this information to evaluate whether use might be appropriate.
- Emodepside topical solution for cats has no efficacy in dogs when administered topically; **it must be administered orally**.
- Drug formulation matters, and each pharmaceutical product is carefully formulated to optimize pharmacokinetics and drug safety; the excipients used for topical products are not intended for oral use and may lead to variability in the pharmacokinetic and safety profiles.
- The suggested dose of emodepside for dogs with MDR *A caninum* isolates is 1 mg/kg PO.
- Emodepside is a known substrate for P-glycoprotein,[32] and dogs with a deletion mutation of the multidrug sensitivity gene (*MDR1* gene, also known as *ABCB1* gene) may be at increased risk for severe adverse effects,[33] especially if they receive incorrect doses of the topical feline product.
- The 1 mg/kg PO dose of emodepside for dogs is one-third of the topical labeled dose for cats, and administering more than this dose may increase the likelihood of adverse effects.
- Given the potential risks of using this product in dogs, emodepside topical solution for cats should only be used in dogs when the poor effectiveness of the triple anthelmintic combination has been previously confirmed via FECRT.
- All FDA requirements and Animal Medicinal Drug Use Clarification Act provisions with regard to extra-label drug use should be closely followed, including informing owners about label warnings and other known risks.

FEC = fecal egg count
FECRT = fecal egg count reduction test
MDR = multidrug-resistant

If FEC reduction is <75%, treatment should be considered ineffective and adjusted to a triple anthelmintic combination with all drugs administered concurrently at the labeled doses. Drugs should be administered sequentially on the same day and not mixed together.

This treatment plan has been successful in eliminating active infections in persistent hookworm cases[26]:

- Febantel (25 mg/kg PO)/pyrantel pamoate (5 mg/kg PO)/praziquantel (5 mg/kg PO) + moxidectin (2.5 mg/kg topical), or
- Fenbendazole (50 mg/kg PO once daily for 3 days) + pyrantel pamoate (5 mg/kg PO) + moxidectin (2.5 mg/kg topical)

Treatment success using this triple-drug combination depends on whether the hookworms are moxidectin-resistant. MDR hookworms studied by the authors were all ivermectin-resistant but may still be moxidectin-sensitive. The aforementioned regimen should be effective if hookworms are moxidectin-sensitive; however, this approach may be ineffective if the infecting source hookworms were previously treated with moxidectin. The authors have diagnosed recent cases of moxidectin-resistant *A caninum* in greyhounds in which monthly moxidectin treatments offered little benefit. If this monthly treatment regimen is effective in eliminating egg shedding, the patient will need to remain on this treatment for several months, or possibly for life, as somatic tissue stores will continually leak and repopulate the intestine for an extended time.

Extra-label administration at higher-than-label doses might improve efficacy, but there are currently no data to support such a recommendation. In addition, some parasitologists recommend repeating moxidectin treatment every 2 weeks for the first 4 treatments, then treating monthly, as this allows the moxidectin to rapidly reach a steady-state tissue concentration due to the long half-life of moxidectin in dogs.[27-29] This is reasonable and

potentially beneficial, although no specific data presently exist. Other products containing moxidectin may also be effective, but there are no published data to support the effectiveness of those products against MDR *A caninum* isolates.

Emodepside

If the triple combination approach is ineffective, emodepside is the only potentially effective alternative treatment, based on a recent study evaluating the efficacy of emodepside and praziquantel against an MDR *A caninum* isolate.[10] Oral emodepside (1 mg/kg) with praziquantel (5 mg/kg) demonstrated an efficacy of 99.6% with a 100% reduction in FEC at 10 days posttreatment.

Emodepside is not currently approved for use in dogs in the United States; however, emodepside (with praziquantel) is FDA-approved as a topical solution for cats. The authors have determined that extra-label use of emodepside topical solution for cats, administered PO at a different dose than is recommended for this product, has high efficacy in MDR *A caninum* isolates refractory to triple combination treatment.

The authors have monitored FEC in 17 client-owned dogs, both greyhounds and nongreyhounds, treated by private practice clinicians using 1 mg/kg PO emodepside administered once. In all cases, FEC reduction was 100% at 14 days, and no adverse effects were observed. However, there are a number of important factors to consider with extra-label emodepside use (see ***Considerations for Extra-Label Emodepside***).

If extra-label use of the emodepside topical solution for cats is warranted, the patient should be fasted overnight prior to administration, and food should not be provided until 4 hours posttreatment. The dose should be given at the clinic and not dispensed to the owner. The product should be drawn into a syringe with a needle; then, the needle should be removed and the syringe administered as distal orally as possible to decrease the ability of the patient to taste the product.

Precise dosing of emodepside is critical and cannot be readily achieved without careful calculations. The correct canine dose cannot be estimated based on the feline label. The product comes in 3 sizes: small cat (5.5 lb [2.5 kg]), medium cat (11 lb [5 kg]), and large cat (17.6 lb [8 kg]), all of which have a different volume but the same concentration of emodepside (21.4 mg/mL). The following formula should be used to determine the correct dose for dogs:

[(weight of dog in kg × 1 mg/kg) ÷ 21.4 mg/mL] = mL of emodepside topical solution for cats to administer PO to a dog

For example, an 8.8-lb (4-kg) dog would receive 0.19 mL, and a 66-lb (30-kg) dog would receive 1.4 mL.

Other Supportive Treatments

The authors have not evaluated nor are aware of any evidence regarding the use of other concurrent and/or supportive treatments (eg, probiotics) and cannot provide recommendations on their use.

Follow-Up & Environmental Hygiene

The authors strongly recommend that FEC (not just flotations) be evaluated monthly to monitor egg shedding.

It is critical that strict environmental hygiene is practiced. Feces of a dog shedding hookworm eggs (or any helminth parasite) should be picked up immediately and properly disposed of to eliminate the potential for reinfection or spread.

Continues ▶

For an instructional guide on the Mini-FLOTAC technique, see **brief.vet/Mini-FLOTAC-Components**

The recommendations made in this article are based on the authors' interpretation of best available evidence at the time of publication and should not be construed as being permanent. As new knowledge is gained and new products become available, recommendations listed here are likely to change.

It takes ≥5 days for hookworm eggs to develop to the infective third-stage larvae in ideal temperature and humidity conditions[30]; therefore, fecal pickup even every few days can be highly effective in preventing environmental contamination. However, waiting can result in feces breakdown, allowing the hookworm larvae (or other parasite eggs/larvae) to contaminate the environment.

If reinfection with ivermectin-resistant worms from the environment is permitted to occur in dogs treated with moxidectin, resistance to moxidectin can rapidly develop.[31]

There are several methods for killing hookworm larvae in the environment, but their effectiveness is undetermined.

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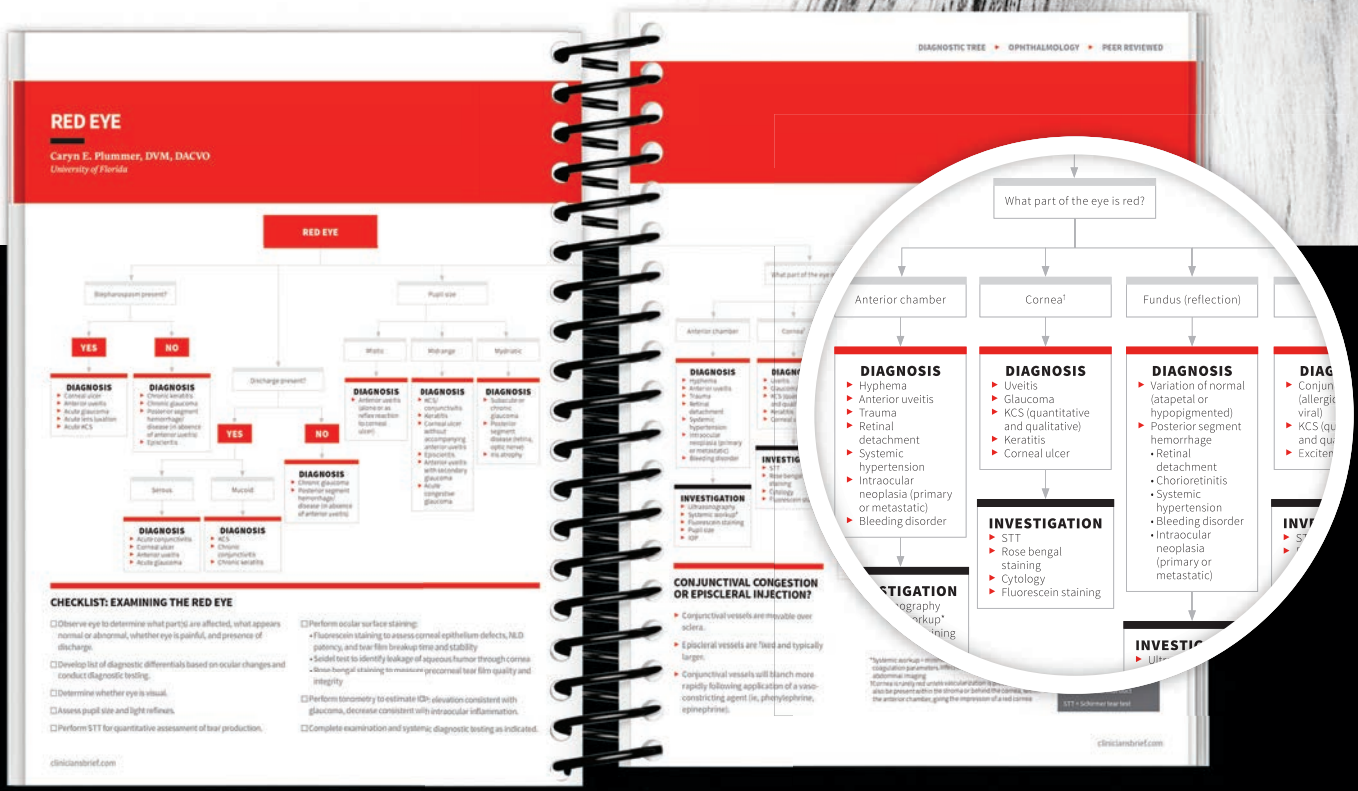

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Baytril® Otic

(enrofloxacin/silver sulfadiazine) Antibacterial-Antimycotic Emulsion

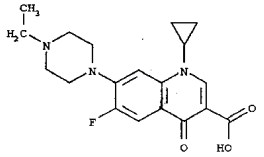
For Ototopical Use In Dogs

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

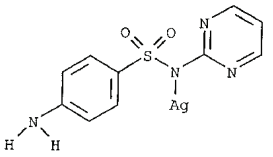
Federal law prohibits the extralabel use of this drug in food-producing animals.

PRODUCT DESCRIPTION:
Each milliliter of Baytril® Otic contains: enrofloxacin 5 mg (0.5% w/v), silver sulfadiazine (SSD) 10 mg (1.0% w/v), benzyl alcohol (as a preservative) and cetylstearyl alcohol (as a stabilizer) in a neutral oil and purified water emulsion. The active ingredients are delivered via a physiological carrier (a nonirritating emulsion).

CHEMICAL NOMENCLATURE AND STRUCTURE:
Enrofloxacin
1-Cyclopropyl-7-(4-ethyl-1-piperazinyl)-6-fluoro-1, 4-dihydro-4-oxo-3-quinolinecarboxylic acid.



Silver Sulfadiazine
Benzenesulfonamide, 4-amino-N-2-pyrimidinyl-monosilver



ACTIONS:
Enrofloxacin, a 4-fluoroquinolone compound, is bactericidal with activity against a broad spectrum of both Gram negative and Gram positive bacteria. Fluoroquinolones elicit their bactericidal activities through interactions with two intracellular enzymes, DNA gyrase (DNA topoisomerase II) and DNA topoisomerase IV, which are essential for bacterial DNA transcription, synthesis and replication. It is believed that fluoroquinolones actively bind with bacterial DNA:ENZYME complexes and thereby inhibit the essential processes catalyzed by the enzymes (DNA supercoiling and chromosomal decatenation).[1] The ultimate outcome of the fluoroquinolone intervention is DNA fragmentation and bacterial cell death.[2,3]
Silver sulfadiazine (SSD) is synthesized from silver nitrate and sodium sulfadiazine.[4] This compound has a wide spectrum of antimicrobial activity against Gram negative and Gram positive bacteria and is also an effective antimycotic.[5,6] SSD suppresses microbial growth through inhibition of DNA replication and modification of the cell membrane.

MICROBIOLOGY:
In clinical field trials, Baytril® Otic demonstrated elimination or reduction of clinical signs associated with otitis externa and *in vitro* activity against cultured organisms. Baytril® Otic is effective when used as a treatment for canine otitis externa associated with one or more of the following organisms: *Malassezia pachydermatis, coagulase-positive Staphylococcus spp., Pseudomonas aeruginosa, Enterobacter spp., Proteus mirabilis, Streptococci spp., Aeromonas hydrophila, Aspergillus spp., Klebsiella pneumoniae,* and *Candida albicans.*
In vitro assays, such as disk-diffusion and agar/broth-dilution, are used to determine the susceptibilities of microbes to antimicrobial therapies. Results of agar/broth-dilution assays are reported as a Minimal Inhibitory Concentration (MIC) which represents the lowest antimicrobial concentration, expressed in µg/mL, capable of inhibiting the growth of a pathogenic microorganism. MICs are used in conjunction with pharmacokinetics to predict the *in vivo* efficacy of systemically administered antimicrobials. Topical administration of Baytril® Otic to an exudate and debris-free canal, however, will generally result in local antimicrobial concentrations that greatly exceed serum and tissue levels resulting from systemic therapy. Therefore, when using Baytril® Otic as a treatment for canine otitis externa, interpret susceptibility data cautiously.

INDICATIONS:
Baytril® Otic is indicated as a treatment for canine otitis externa complicated by bacterial and fungal organisms susceptible to enrofloxacin and/or silver sulfadiazine (see Microbiology section).

EFFECTIVENESS:
Due to its combination of active ingredients, Baytril® Otic provides antimicrobial therapy against bacteria and fungi (which includes yeast) commonly encountered in cases of canine otitis externa.

The effectiveness of Baytril® Otic was evaluated in a controlled, double-blind, multi-site clinical trial. One hundred and sixty-nine dogs (n=169), with naturally occurring active otitis externa participated in the study. The presence of active disease was verified by aural cytology, microbial culture and otoscopy/clinical scoring. Qualified cases were randomly assigned to either Baytril Otic treatment (n=113) or to a comparable placebo-based regimen (n=56). Treatments were administered twice daily for up to 14 days. Assessment of effectiveness was based on continued resolution of clinical signs 3 to 4 days following administration of the last dose.
At study conclusion, Baytril® Otic was found to be a significantly more effective treatment for canine otitis externa than the placebo regimen. Based on the scoring system used to assess treatment response, therapeutic success occurred in 67% of Baytril® Otic-treated infections compared to 14% with placebo (r-value^2 0.001) after 14 days of treatment.

CONTRAINDICATIONS:
Baytril® Otic is contraindicated in dogs with suspected or known hypersensitivity to quinolones and/or sulfonamides.

HUMAN WARNINGS:
Not for human use. Keep out of the reach of children. Avoid contact with eyes. In case of contact, immediately flush eyes with copious amounts of water for 15 minutes. In case of dermal contact, wash skin with soap and water. Consult a physician if irritation develops or persists following ocular or dermal exposures. Individuals with a history of hypersensitivity to quinolone compounds or antibacterials should avoid handling this product. In humans, there is a risk of user photosensitization within a few hours after excessive exposure to quinolones. If excessive accidental exposure occurs, avoid direct sunlight.

PRECAUTIONS:
The use of Baytril® Otic in dogs with perforated tympanic membranes has not been evaluated. Therefore, the integrity of the tympanic membrane should be evaluated before administering this product. If hearing or vestibular dysfunction is noted during the course of treatment, discontinue use of Baytril® Otic.
Quinolone-class drugs should be used with caution in animals with known or suspected Central Nervous System (CNS) disorders. In such animals, quinolones have, in rare instances, been associated with CNS stimulation which may lead to convulsive seizures.
Quinolone-class drugs have been associated with cartilage erosions in weightbearing joints and other forms of arthropathy in immature animals of various species.
The safe use of Baytril® Otic in dogs used for breeding purposes, during pregnancy, or in lactating bitches, has not been evaluated.

ADVERSE REACTIONS:
During clinical trials, 2 of 113 (1.7%) dogs exhibited reactions that may have resulted from treatment with Baytril® Otic. Both cases displayed local hypersensitivity responses of the aural epithelium to some component within the Baytril® Otic formulation. The reactions were characterized by acute inflammation of the ear canal and pinna.
For medical emergencies or to report adverse reactions, call 1-800-422-9874. For customer service or to obtain product information, including Material Safety Data Sheet, call 1-800-633-3796.

SAFETY:
General Safety Study:
In a target animal safety study, Baytril® Otic was administered in both ears of 24 clinically normal beagle dogs at either recommended or exaggerated dosages: 10, 30 or 50 drops applied twice daily for 42 consecutive days. A control group of 8 beagle dogs was treated by administering 50 drops of vehicle in one ear twice daily for 42 consecutive days, with the contralateral ear untreated. Erythema was noted in all groups, including both treated and untreated ears in the controls, which resolved following termination of treatment.

Oral Safety Study:
In order to test safety in case of ingestion, Baytril® Otic was administered, twice daily for 14 consecutive days, to the dorsum of the tongue and to the left buccal mucosa of 6 clinically normal dogs. No adverse local or systemic reactions were reported.

DOSAGE AND ADMINISTRATION:
Shake well before each use.
Tilt head so that the affected ear is presented in an upward orientation. Administer a sufficient quantity of Baytril® Otic to coat the aural lesions and the external auditory canal. As a general guide, administer 5-10 drops per treatment in dogs weighing 35 lbs. or less and 10-15 drops per treatment in dogs weighing more than 35 lbs. Following treatment, gently massage the ear so as to ensure complete and uniform distribution of the medication throughout the external ear canal. Apply twice daily for a duration of up to 14 days.

STORAGE:
Store between 4° and 25°C (40 - 77°F). Store in an upright position. Do not store in direct sunlight.

HOW SUPPLIED:
Baytril® Otic (enrofloxacin/silver sulfadiazine)

Size	Presentation
15 mL	Oval plastic bottle with dropper tip and extended tip closure

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1 **CASE IN POINT** **PAGE 11**

Which of the following statements about sterile steroid-responsive lymphadenopathy is *false*?

A. Clinical signs may vary.
B. Only internal lymph nodes are affected.
C. Most patients respond to glucocorticoid therapy.
D. Relapses may occur.

2 **TOP 5** **PAGE 17**

Brachycephalic dogs are how many more times likely to be affected by corneal ulcers as compared with nonbrachycephalic dogs?

A. 1 to 2
B. 3 to 5
C. 7 to 10
D. 11 to 20

3 **CONSULT THE EXPERT** **PAGE 30**

If environmental cleaning is regularly performed while a dermatophytosis patient is receiving topical therapy, most homes can be decontaminated with _____ cleanings after cure.

A. 1 or 2
B. 3 or 4
C. 5 or 6
D. 7 or 8

4 **MANAGEMENT TREE** **PAGE 59**

When performing a fecal egg count reduction test, how many days after treatment should the posttreatment fecal egg count be performed?

A. 1 to 3
B. 5 to 7
C. 10 to 14
D. 14 to 21

5 **CONSULT THE EXPERT** **PAGE 61**

In ideal temperature and humidity conditions, how many days does it take hookworm eggs to develop into third-stage infective larvae?

A. <3 days
B. <5 days
C. <7 days
D. <10 days

Answer Key:
1: B 2: D 3: A 4: C 5: B

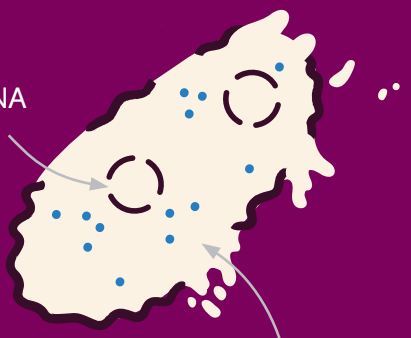
Baytril® Otic

(enrofloxacin/silver sulfadiazine) Emulsion

Your go-to for fighting *Pseudomonas* ear infections

ENROFLOXACIN

- Attacks on the inside
- Destroys bacterial DNA
- Effective against Gram (+) cocci and Gram (–) rods



SILVER SULFADIAZINE

- Attacks on the outside
- Breaks down cell walls/membranes
- Effective against Gram (+) cocci, Gram (–) rods and budding yeast

DEEP-REACHING ACTION
NON-IRRITATING

Only Baytril® Otic (enrofloxacin/silver sulfadiazine) Emulsion fights *Pseudomonas* with two mechanisms of action.

Stock Baytril® Otic for your toughest otitis externa cases.

CAUTION: Available only from a licensed veterinarian. Federal law prohibits the extra-label use of this drug in food-producing animals. **PRECAUTIONS:** The safe use of Baytril® Otic in dogs used for breeding purposes, during pregnancy, or in lactating bitches has not been evaluated. The use of Baytril® Otic in dogs with perforated tympanic membranes has not been evaluated. Therefore, the integrity of the tympanic membrane should be evaluated before administering this product. If hearing or vestibular dysfunction is noted during the course of treatment, discontinue use of Baytril® Otic. **CONTRAINDICATIONS:** Baytril® Otic is contraindicated in dogs with suspected or known hypersensitivity to quinolones and/or sulfonamides.

See page 70 for product information summary.

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BOEHRINGER INGELHEIM'S SHOTS FOR GOOD℠ PROGRAM

Boehringer Ingelheim is partnering with GreaterGood.org to join the fight against rabies in Puerto Rico. Over the next 3 years, Boehringer Ingelheim will donate IMRAB® *doses and rabies seals to help prevent rabies in 60,000 dogs and cats.*

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[1] Stray animal population booming in post-hurricane Puerto Rico. https://commmedia.psu.edu/news/story/stray-animal-population-booming-in-post-hurricane-puerto-rico. Accessed on July 26, 2019.

[2] Data on file.

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