July 2018

clinician's brief

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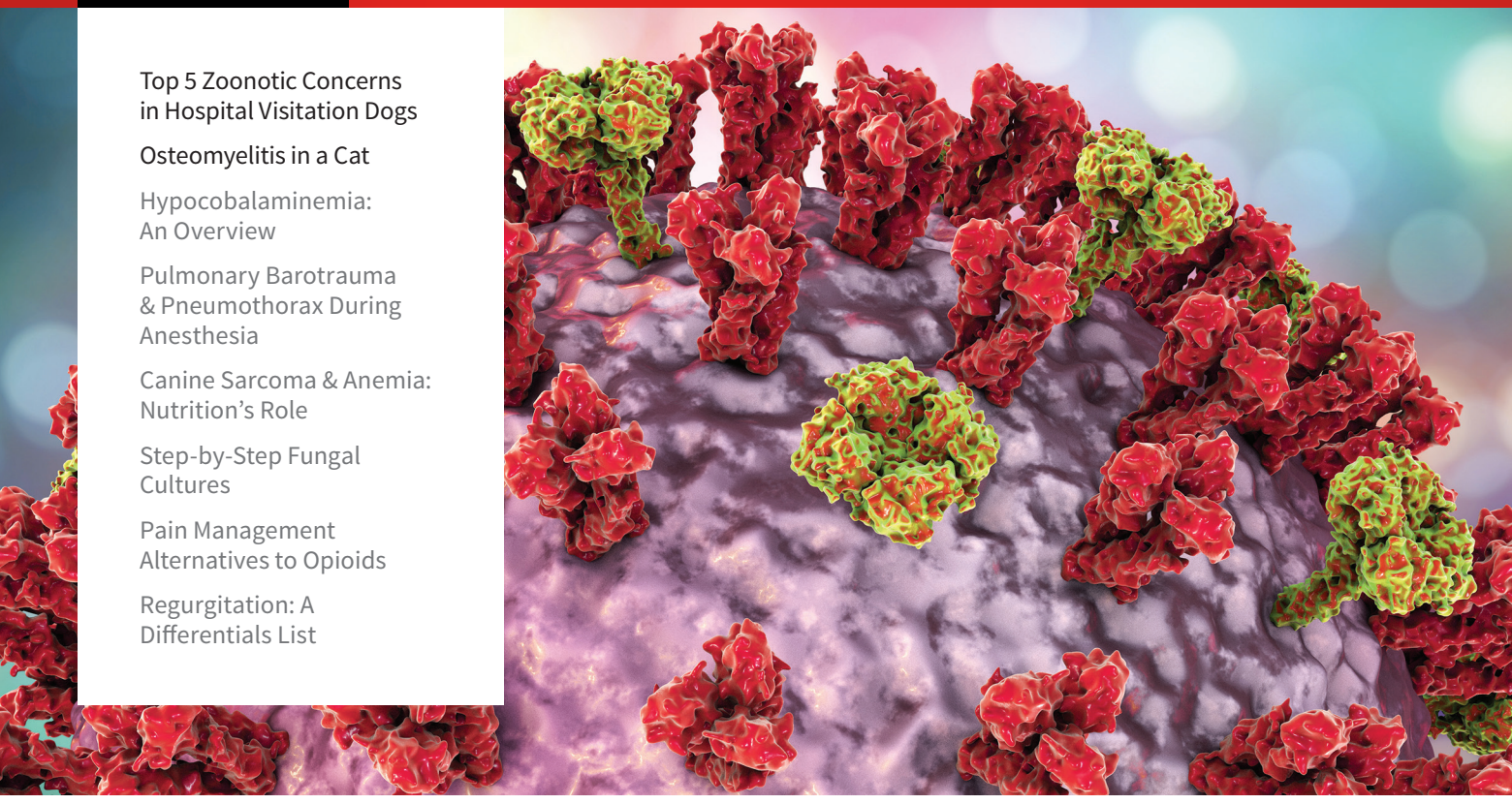
EMERGING INFECTIOUS DISEASES

IN THIS ISSUE



Volume 16 Number 7

WSAVA Global Veterinary Community

clinician's brief
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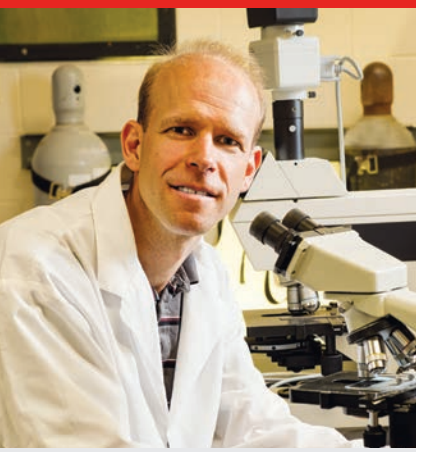

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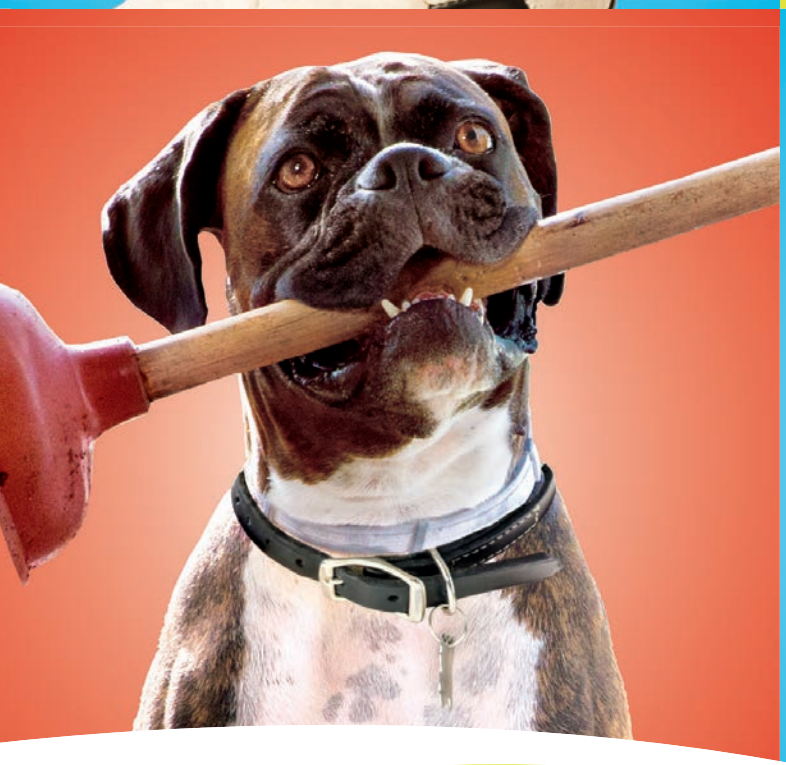

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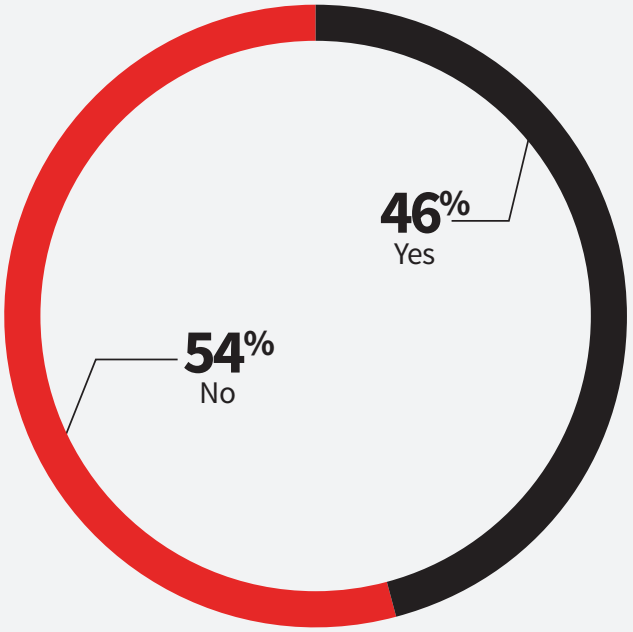

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24

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9

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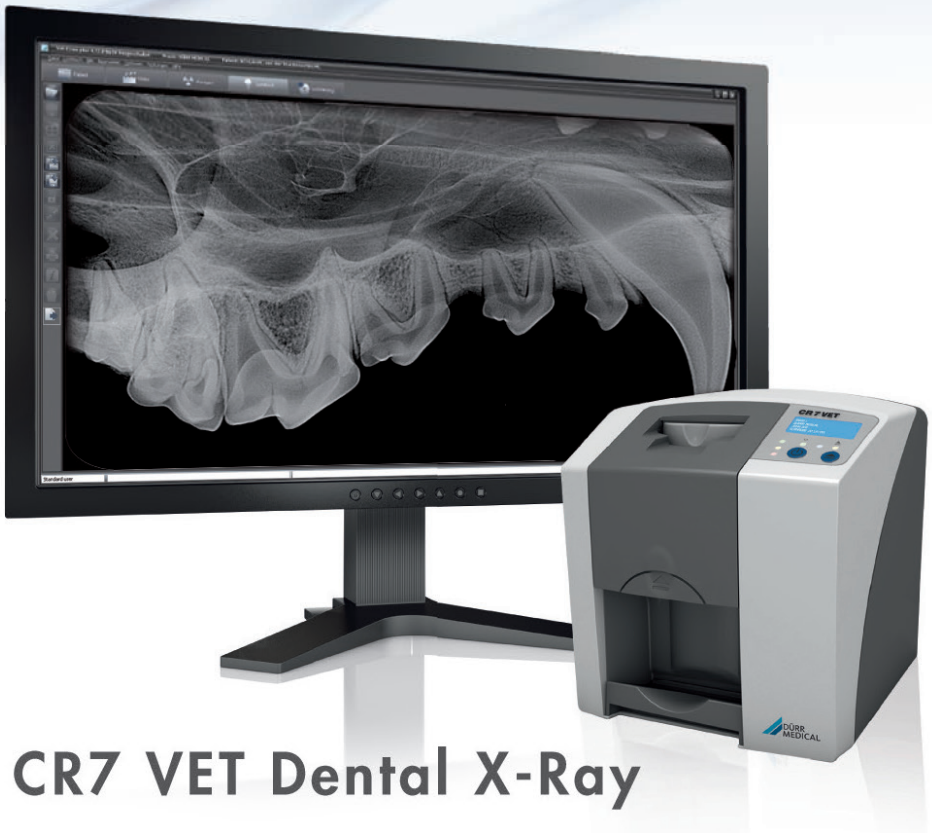

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[2]Levy S., Millership J., et al. (2010). Confirmation of presence of Borrelia burgdorferi outer surface protein C antigen and production of antibodies to Borrelia burgdorferi outer surface protein C in dogs vaccinated with a whole-cell Borrelia burgdorferi bacterin. *Intern J Appl Res Vet Med.* 8(3), 123–128.

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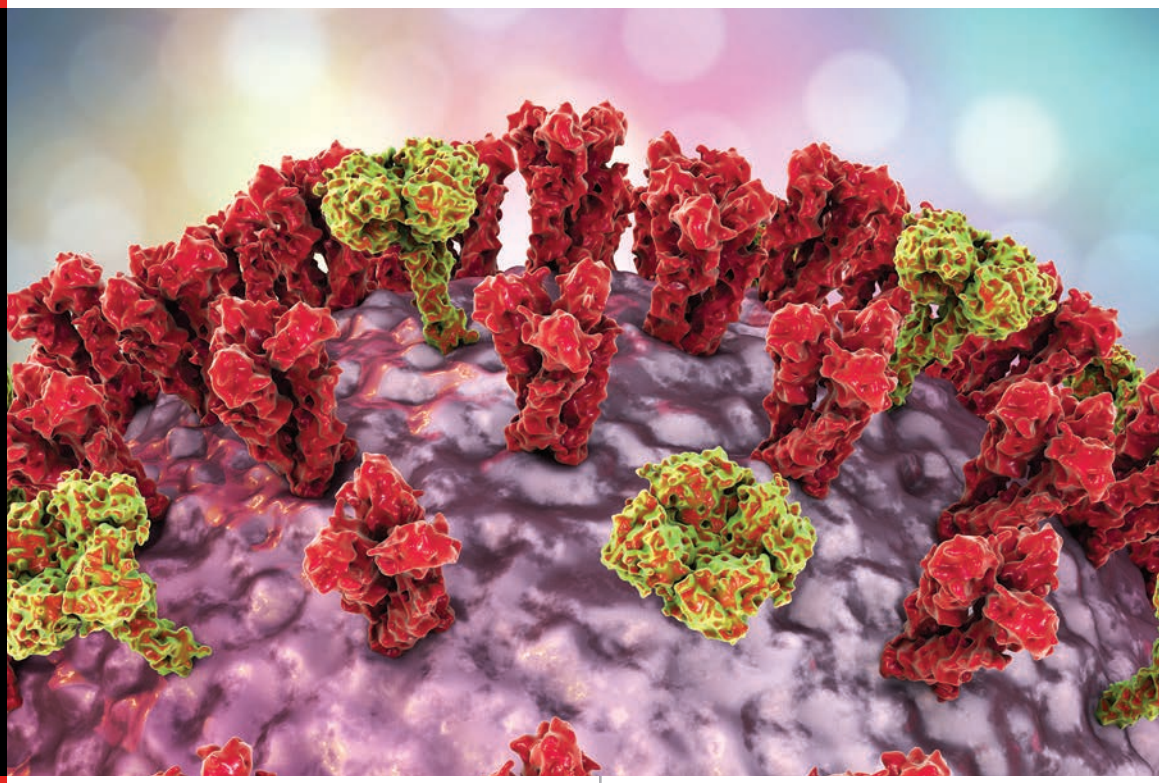
The Veterinary Significance of Emerging Infectious Diseases
J. Scott Weese, DVM, DVSc, DACVIM

PG 14



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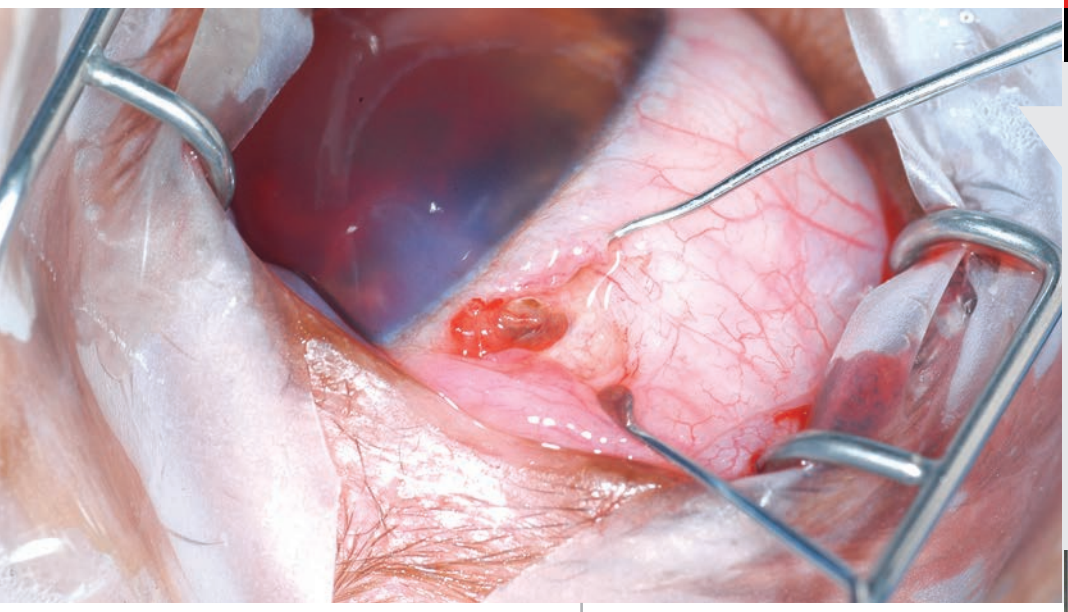

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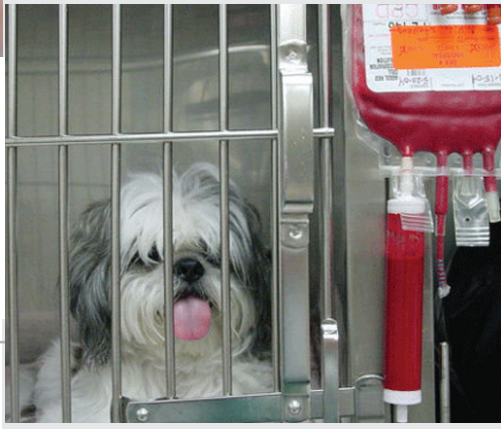

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CASE IN POINT PAGE 26

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DIFFERENTIAL DIAGNOSIS PAGE 21

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PROCEDURES PRO PAGE 31

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CONSULT THE EXPERTS PAGE 65

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SPECIAL REPORT PAGE 48

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PROCEDURES PRO PAGE 31

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SPECIAL REPORT PAGE 48

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DIET IN DISEASE PAGE 53

Continues on page 12


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CASE IN POINT PAGE 26

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CONSULT THE EXPERTS PAGE 65

DIFFERENTIAL DIAGNOSIS PAGE 21

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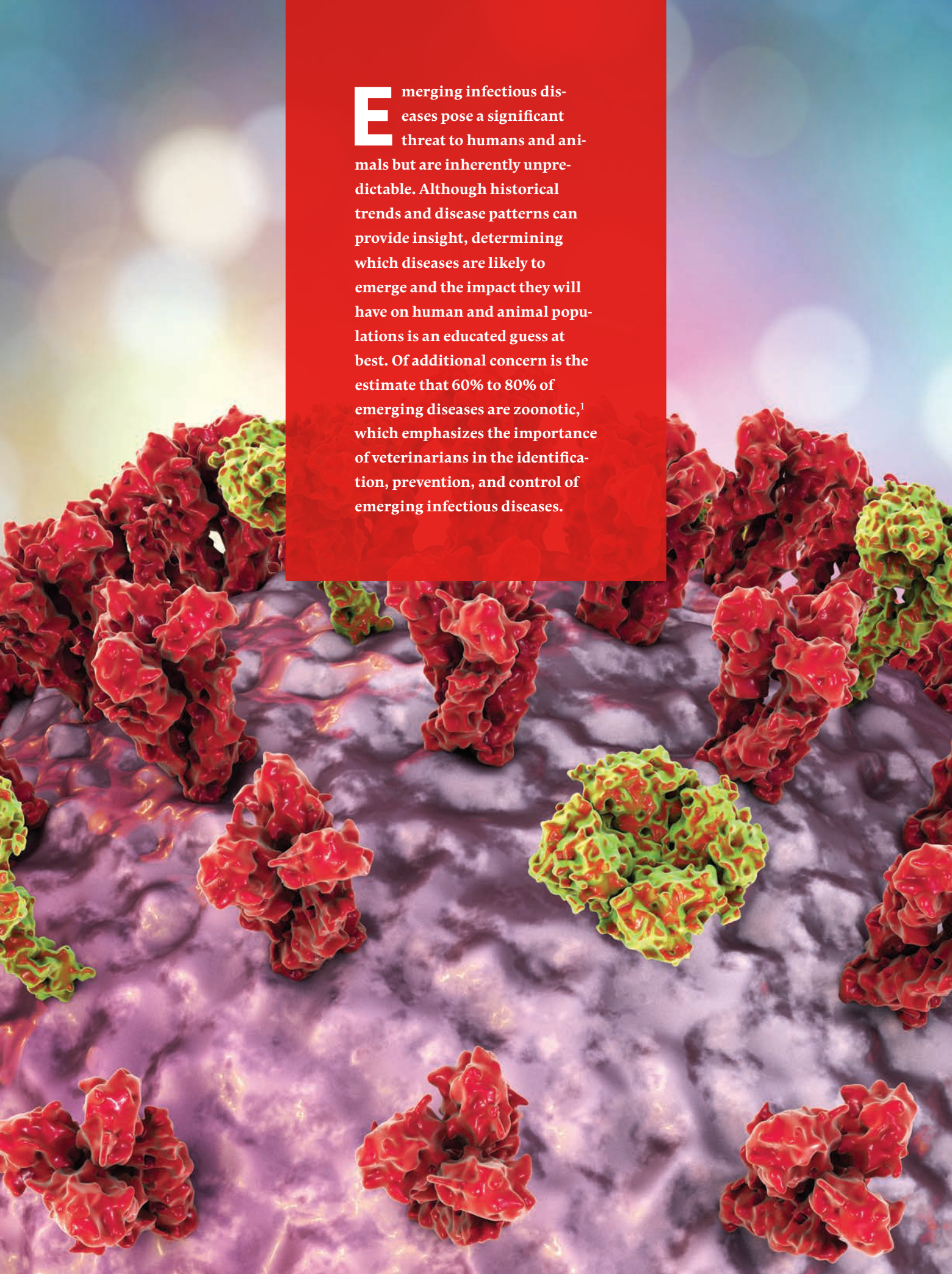
THE VETERINARY SIGNIFICANCE OF EMERGING INFECTIOUS DISEASES

J. Scott Weese, DVM, DVSc, DACVIM
Ontario Veterinary College



Emerging infectious diseases pose a significant threat to humans and animals but are inherently unpredictable. Although historical trends and disease patterns can provide insight, determining which diseases are likely to emerge and the impact they will have on human and animal populations is an educated guess at best. Of additional concern is the estimate that 60% to 80% of emerging diseases are zoonotic,[1] which emphasizes the importance of veterinarians in the identification, prevention, and control of emerging infectious diseases.

An ecosystem approach to health considers disease occurrence to be at the intersection of the microbial agent, the host (human or animal), and the environment.[1] Any alterations in the agent, host, or environment can alter the risk for disease. Thus, new infectious disease threats can emerge from a variety of sources.

Emergence of New Pathogens

Emergence of new pathogens is uncommon but continues to occur. If highly transmissible, new pathogens can have profound effects, as the worldwide population would be immunologically naïve to the emerging pathogen. For example, the emergence of canine parvovirus in the 1970s[2] became a worldwide epidemic, with rapid international transmission and high morbidity and mortality rates.

Canine influenza is a more recent example of the threats posed by emerging pathogens. The emergence of equine-origin canine influenza H3N8 in the United States in the early 2000s[3] demonstrated the potential impact of antigenic shift of influenza on the canine population. The more recent emergence of avian-origin canine influenza H3N2 caused—and continues to cause—widespread illness and disruption in parts of Asia, the United States, and Canada.[4,5]

If highly transmissible, new pathogens can have profound effects, as the worldwide population would be immunologically naïve to the emerging pathogen.

Change in Existing Pathogens

Alterations in existing pathogens can impact a pathogen's virulence (eg, acquisition of new virulence factors) and the ability to treat (eg, acquisition of antimicrobial-resistant genes or antiviral resistance) or prevent disease (eg, alterations in vaccine efficacy, resistance to heartworm prophylaxis). The worldwide epidemic of antimicrobial resistance, particularly methicillin-resistant staphylococci[6] and extended-spectrum β-lactamase production in gram-negative bacteria, has had tremendous impacts on human and animal populations.[7] Multidrug-resistant pathogens cause large numbers of infections every year and can be associated with higher morbidity and mortality rates; the need for more expensive, toxic, or cumbersome treatments; and the risk for transmission to other humans or animals. Economic impacts are similarly profound; the World Bank has estimated that by 2050 the global burden of antimicrobial resistance could surpass that of the 2008 financial crisis.[8] New resistance mechanisms, including resistance to "last-resort" drugs such as colistin,[9] continue to be identified and will continue to pose a problem to the veterinary profession as bacterial evolution outpaces antimicrobial development.

Development of Virulence

Virulence may develop through an existing but typically nonpathogenic microbe. *Elizabethkingia anophelis* is an example of such virulence development in humans; the risk in animals is unknown. This gram-negative bacterium is widespread in the environment and was considered innocuous until clusters of serious infections were identified in humans, primarily immunocompromised humans in hospitals, in various countries.[10] The reasons for this change are unclear. Although *E anophelis* infection has not been reported in animals, it is possible that there is some degree of risk for infection. Regardless, *E anophelis* highlights the potential for organ-

isms that were previously considered to be ubiquitous and innocuous to cause disease.

Change in the Range of Existing Pathogens

Many pathogens have well defined ranges that may be limited by geography and control measures (eg, rabies), vector ranges (eg, *Borrelia burgdorferi*), reservoir host ranges (eg, *Cytauxzoon felis*), and climate (eg, various parasites). Changes in any of these limiting factors can result in the potential for range expansion. Range expansion can also occur through human activities (eg, international movement of humans and animals) and accidental international transportation of pests and, thus, the pathogens they carry. Although of limited consequence in dogs and cats, introduction of West Nile virus through a route that is still unknown resulted in establishment of this foreign mosquito-borne virus in North America, and the impacts of this disease on humans and some animal populations are ongoing.[11-15]

Expanding ranges of various vector-borne diseases are particularly noteworthy. In North America, tick ranges have been expanding due in part to climate change.[16] When reservoir hosts move in parallel with vectors or when competent hosts are already present in the expansion regions, vector-borne pathogens may spread with the vectors, as shown by the steady movement of Lyme disease into the northern and western United States and into Canada.[17] Such movement highlights the need for predictive modeling to identify new threats and the need for awareness of disease threats in adjacent regions.

New Human Encounters in Remote Endemic Ranges

Various pathogens presumably exist in remote sites where there is little human presence. There are still regions of the world that have had limited human exposure, particularly parts of sub-Saharan Africa and regions of the Amazon basin. With the remarkable biodiversity in these areas, expansion of humans and their animals into these areas may result in exposure to pathogens considered new to the region.

Apparent emergence of a disease may sometimes simply reflect advances in diagnostic testing.

Ability to Diagnose

Apparent emergence of a disease may sometimes simply reflect advances in diagnostic testing. For example, *Bartonella* spp can be difficult to identify. As new methods for detection have become available, members of this genus have been increasingly implicated in a variety of diseases.[18]

Advances in laboratory methods that allow for rapid, cost-effective detection of all microorganisms in a sample, including previously unknown bacteria and viruses, have made it possible to identify unknown microorganisms rapidly and at low cost. This has led to identification of myriad "new" viruses.[19-21] Humans and animals have extensive commensal virome populations, and the ability to identify new viruses currently outpaces the ability to interpret the relevance of these discoveries. A high-profile example is the identification of canine circovirus. After reports of this virus and the subsequent ability to test for it first emerged, there was widespread concern about canine circovirus as a cause of serious enteric disease in dogs; however, proof of its role as a primary pathogen is still

lacking.[22-24] This highlights the potential confusion that can be associated with availability of new diagnostic tests when the clinical relevance of the results is unclear.

Change in Host Susceptibility

A change in host susceptibility has been exemplified in medicine early in the era of human immunodeficiency virus (HIV) and acquired immune deficiency syndrome (AIDS). Before effective HIV management approaches were available, progression to end-stage AIDS resulted in profoundly immunocompromised individuals, which led to identification of a range of previously rare or unknown infectious diseases caused by organisms that were predominantly or only pathogenic in these highly compromised hosts (see ***Suggested Reading***).[25-29] Such a severely compromising and widespread disease is not currently recognized in animals; however, emergence of new secondary pathogens in humans with AIDS demonstrates the potential for disease caused by a range of novel or overlooked microorganisms associated with the emergence of new, highly susceptible patient populations. It also emphasizes the challenges that might be posed by advances in veterinary care (eg, treatment of cancer or immune-mediated disease) that can prolong the life of patients but increase their risk for infection from existing and emerging pathogens.

AIDS = acquired immune deficiency syndrome

HIV = human immunodeficiency virus

New infectious disease issues will pose threats to animal and, potentially, human populations.

The Future

Logical estimations and models for emergence can be developed, but emergence is ultimately unpredictable. New infectious disease issues will pose threats to animal and, potentially, human populations. Infectious diseases of current significance may not have been recognized or considered important 5 to 10 years ago, and infectious diseases that will be significant 10 years from now may not be currently recognized or considered important, illustrating the dynamic nature of disease.

References

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Suggested Reading

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See page 19 for product information summary.

Regurgitation

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University of Tennessee

FOR MORE
Find more Differential Diagnosis lists in upcoming issues of *Clinician's Brief*!

- **Epistaxis**
- **Hypoglycemia**
- **Increased Total Thyroxine**
- **Decreased Total Thyroxine**

Following are differential diagnoses, listed in order of likeliness, for patients presented with regurgitation.

- Esophagitis
- Focal or generalized megaesophagus
  - Focal
    - Vascular ring anomaly
    - Esophageal stricture
  - Generalized
    - Esophageal stricture (if close to lower esophageal sphincter)
    - Hypoadrenocorticism
    - Myasthenia gravis
    - Lead poisoning
    - Botulism
    - Tetanus
    - Hypothyroidism
    - Polyradiculitis
    - Thallium toxicity
- Structural esophageal disease
  - Foreign body
  - Extra- or intraesophageal neoplasia
  - Diverticula
  - Granuloma
    - Fungal
    - *Spirocerca lupi*
- Polymyopathy
- Polyneuropathy
- Organophosphate toxicity
- Hiatal hernia
- Distemper
- *Neospora caninum*

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sentinel® spectrum®

(milbemycin oxime·lufenuron·praziquantel)

Caution

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

Description

SENTINEL® SPECTRUM® is available in four strengths in color-coded packages for oral administration to dogs and puppies according to their weight. Each chewable flavored tablet is formulated to provide a minimum of 0.23 mg/pound (0.5 mg/kg) of milbemycin oxime, 4.55 mg/pound (10 mg/kg) of lufenuron, and 2.28 mg/pound (5 mg/kg) of praziquantel.

Milbemycin oxime consists of the oxime derivatives of 5-didehydromilbemycins in the ratio of approximately 80% A_4 ($C_{32}H_{45}NO_7$, MW 555.71) and 20% A_3 ($C_{31}H_{43}NO_7$, MW 541.68). Milbemycin oxime is classified as a macrocyclic anthelmintic.

Lufenuron is a benzoylphenylurea derivative with the following chemical composition: N-[2,5-dichloro-4-(1,1,2,3,3,3, -hexafluoropropoxy)-phenyl-aminocarbonyl]-2,6- difluorobenzamide ($C_{17}H_8Cl_2F_8N_2O_3$, MW 511.15). Benzoylphenylurea compounds, including lufenuron, are classified as insect development inhibitors (IDIs).

Praziquantel is an isoquinolone anthelmintic with the chemical name 2- (Cyclohexylcarbonyl)-1,2,3,6,7,-11b-hexahydro-4H-pyrazino[2,1-a]isoquinolin-4-one.

Indications

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

Dosage and Administration

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

Dosage Schedule

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

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

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

Heartworm Prevention:

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

Flea Treatment and Prevention:

Treatment with SENTINEL SPECTRUM may begin at any time of the year, preferably starting one month before fleas become active and continuing monthly through the end of flea season. In areas where fleas are common year-round, monthly treatment with SENTINEL SPECTRUM 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 protection product, as necessary.

Intestinal Nematode and Cestode Treatment and Control:

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

Contraindications

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

Warnings

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

Precautions

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

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

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

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

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

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

Adverse Reactions

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

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

For technical assistance call Virbac at 1-800-338-3659.

Information for Owner or Person Treating Animal:

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

Effectiveness

Heartworm Prevention:

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

Intestinal Nematodes and Cestodes Treatment and Control:

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

Flea Prevention and Control

In well-controlled studies, SENTINEL SPECTRUM was effective in preventing flea eggs from hatching, thus providing control of the development of flea populations (*Ctenocephalides felis*).

Palatability

In a field study of 117 dogs offered SENTINEL SPECTRUM, 113 dogs (96.6%) accepted the product when offered from the hand as if a treat, 2 dogs (1.7%) accepted it from the bowl with food, 1 dog (0.9%) accepted it when it was placed in the dog's mouth, and 1 dog (0.9%) refused it.

Animal Safety

In a margin of safety study, 40 ten-week-old puppies (10 per group) were administered either a sham dose (0X) or doses of 1, 3, or 5X the maximum exposure dose of SENTINEL SPECTRUM once every two weeks for a total of seven treatments. Transient ataxia, lethargy, tremors, and salivation were seen in the 3X and 5X groups following each of the seven doses. Lethargy and ataxia were occasionally reported in sham-dosed (0X) and 1X dogs. Tremors were observed twice post-treatment in the 1X treatment group. Vomiting was seen in all treatment groups but at a higher incidence in the 3X and 5X groups. At the 5X dose, shallow breathing was noted in two dogs and one dog was unable to stand following two different doses. All clinical signs resolved within 24 hours.

In a second margin of safety study, 64 six-week-old puppies (16 per group) were dosed with either a sham dose (0X) or 1, 3, or 5X the maximum exposure dose of SENTINEL SPECTRUM on days 1, 15, 29, and 43. A dose-dependent increase in ataxia, decreased activity, tremors, and salivation was seen within 24 hours of treatment. Splayed hind limbs were observed once in one dog in the 5X treatment group. Vomiting was observed in the 5X treatment group.

For SENTINEL SPECTRUM the maximum exposure based on product dosing is 2.5 mg/kg for milbemycin oxime, 50.7 mg/kg for lufenuron and 25.1 mg/kg for praziquantel, which is higher than the minimum effective dose used in the safety studies for milbemycin oxime and lufenuron (see below).

Milbemycin Oxime:

Two studies were conducted in heartworm-infected dogs treated with milbemycin oxime. Mild, transient hypersensitivity reactions were observed in dogs with high microfilariae counts (see **PRECAUTIONS**).

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

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

A rising-dose safety study conducted in rough-coated Collies resulted in ataxia, pyrexia, and periodic recumbency in one of fourteen dogs administered milbemycin oxime at 12.5 mg/kg (5X the maximum exposure dose of SENTINEL SPECTRUM). Prior to receiving the 12.5 mg/kg dose on day 56 of the study, all animals had undergone a dosing regimen consisting of 2.5 mg/kg milbemycin oxime on day 0, followed by 5.0 mg/kg on day 14, and 10.0 mg/kg on day 32. No adverse reactions were observed in any of the Collies treated with doses less than 12.5 mg/kg.

Lufenuron:

In a ten-month study, doses of lufenuron up to 2X the maximum exposure dose of SENTINEL SPECTRUM (10 mg/kg) caused no overt toxicity. A single dose of 200 mg/kg had no marked effect on adult dogs, but caused decreased activity and reduced appetite in eight-week-old puppies. Lufenuron tablets were evaluated with concurrent administration of flea adulticides containing carbaryl, permethrin, chlorpyriphos, and cythioate. No toxicity resulted from these combinations. Lufenuron tablets did not cause cholinesterase inhibition nor did they enhance cholinesterase inhibition caused by exposure to organophosphates.

Two laboratory and two well-controlled field studies were conducted to evaluate reproductive safety of lufenuron tablets in breeding dogs. In one of the laboratory studies, in which lufenuron was administered to Beagle dogs as three divided doses, equivalent to 17.8X the maximum exposure dose of SENTINEL SPECTRUM (10 mg/kg), the ratio of gravid females to females mated was 8/8 or 100% in the control group and 6/9 or 67% in the lufenuron-treated group. The mean number of pups per litter was two animals higher in the lufenuron versus control groups and the mean birth weights of pups from treated bitches in this study was lower than control groups. These pups grew at a similar rate to the control pups. The incidence of nasal discharge, pulmonary congestion, diarrhea/dehydration, and sluggishness was higher in the lufenuron-treated pup group than in the control pup group. The incidence of these signs was transient and decreasing by the end of lactation.

Results from three additional reproductive safety studies, one laboratory and two field studies, evaluating eleven breeds of dogs, did not demonstrate any adverse findings for the reproductive parameters measured, including fertility, pup birth weights, and pup clinical signs, after administration of lufenuron up to 1X the maximum exposure dose of SENTINEL SPECTRUM. The average milk: blood concentration ratio was approximately 60 (i.e., 60X higher drug concentrations in the milk compared to drug levels in the blood of treated bitches). Nursing puppies averaged 8-9 times higher blood concentrations of lufenuron compared to their dams.

Storage Information

Store in a dry place at controlled room temperature, between 59° and 77°F (15-25°C).

How Supplied

SENTINEL SPECTRUM is available in four strengths, formulated according to the weight of the dog. Each strength is available in color-coded packages of six or twelve chewable tablets each.

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

NADA #141-333, Approved by FDA

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sentinel® flavor tabs®

(milbemycin oxime·lufenuron)

The palatable once-a-month prescription tablet that prevents heartworm disease and flea populations in dogs and puppies. SENTINEL® (milbemycin oxime/lufenuron) FLAVOR TABS® also control flea populations and adult hookworms, and remove and control adult roundworm and whipworm infections in dogs and puppies.

Caution

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

Warnings

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

Description

SENTINEL FLAVOR TABS are available in four tablet sizes in color-coded packages for oral administration to dogs and puppies according to their weight. (See Dosage Section). Each tablet is formulated to provide a minimum of 0.23 mg/pound (0.5 mg/kg) of milbemycin oxime and 4.55 mg/pound (10 mg/kg) body weight of lufenuron.

Milbemycin oxime consists of the oxime derivatives of 5-didehydromilbemycins in the ratio of approximately 80% A4 (C32H45NO7, MW 555.71) and 20% A3 (C31H43NO7, MW 541.68). Milbemycin oxime is classified as a macrocyclic anthelmintic.

Lufenuron is a benzoylphenylurea derivative with the following chemical composition: N-[2,5-dichloro-4-(1,1,2,3,3,3, -hexafluoropropoxy)-phenylaminocarbonyl]-2,6- difluorobenzamide (C17H8C12F8N2O3, MW551.15). Benzoylphenylurea compounds, including lufenuron, are classified as insect development inhibitors (IDIs).

Mode of Action

Milbemycin oxime, one active ingredient in SENTINEL FLAVOR TABS, is a macrocyclic anthelmintic which is believed to act by interfering with invertebrate neurotransmission. Milbemycin oxime eliminates the tissue stage of heartworm larvae and the adult stage of hookworm (Ancylostoma caninum), roundworm (Toxocara canis and Toxascaris leonina) and whipworm (Trichuris vulpis) infestations when administered orally according to the recommended dosage schedule.

Lufenuron, the other active ingredient in SENTINEL FLAVOR TABS, is an insect development inhibitor which breaks the flea life cycle by inhibiting egg development. Lufenuron's mode of action is interference with chitin synthesis, polymerization and deposition. Lufenuron has no effect on the adult flea. After biting a lufenuron-treated dog, the female flea ingests a blood meal containing lufenuron which is subsequently deposited in her eggs. Lufenuron prevents most flea eggs from hatching or maturing into adults and thus prevents and controls flea populations by breaking the life cycle. (See Efficacy).

Indications

SENTINEL FLAVOR TABS are indicated for use in dogs and puppies, four weeks of age and older, and two pounds body weight or greater. SENTINEL FLAVOR TABS are also indicated for the prevention of heartworm disease caused by Dirofilaria immitis for the prevention and control of flea populations, the control of adult Ancylostoma caninum (hookworm), and the removal and control of adult Toxocara canis and Toxascaris leonina (roundworm) and Trichuris vulpis (whipworm) infections.

Lufenuron controls flea populations by preventing the development of flea eggs and does not kill adult fleas. Concurrent use of an adulticide product may be necessary for adequate control of adult fleas.

Without concurrent use of an adulticide, adequate flea control may not be achieved in dogs that have repeated exposure to flea infested animals or environments.

Precautions

Do not use in puppies less than four weeks of age and less than two pounds of body weight. Prior to administration of SENTINEL FLAVOR TABS, dogs should be tested for existing heartworm infections. Infected dogs should be treated to remove adult heartworms and microfilariae prior to initiating treatment with SENTINEL FLAVOR TABS. Mild, transient hypersensitivity reactions manifested as labored respiration, vomiting, salivation and lethargy have been noted in some treated dogs carrying a high number of circulating microfilariae. These reactions are presumably caused by release of protein from dead or dying microfilariae.

SENTINEL FLAVOR TABS immediately break the flea life cycle by inhibiting egg development. However, preexisting flea populations may continue to develop and emerge after treatment with SENTINEL FLAVOR TABS has begun. Based on results of clinical studies, this emergence generally occurs during the first 30-60 days. Therefore, noticeable control may not be observed until several weeks after dosing when a preexisting infestation is present. Cooler geographic areas may have longer lag periods due to a prolonged flea life cycle. The concurrent use of an approved adulticide may be employed depending on the severity of the infestation.

If a SENTINEL FLAVOR TABS-treated dog comes in contact with a flea-infested environment, adult fleas may infest the treated animal. These adult fleas are unable to produce viable offspring. The temporary use of an adulticide product may be necessary to kill these adult fleas.

Efficacy: Milbemycin Oxime

Milbemycin oxime provided complete protection against heartworm infection in both controlled laboratory and clinical trials.

In laboratory studies, a single dose of milbemycin oxime at 0.5 mg/kg was effective in removing roundworm, hookworm and whipworm. In well-controlled clinical trials, milbemycin oxime was also effective in removing roundworms and whipworms and in controlling hookworms.

Efficacy: Lufenuron

Lufenuron provided 99% control of flea egg development for 32 days following a single dose of lufenuron at 10 mg/kg in studies using experimental flea infestations. In well-controlled clinical trials, when treatment with lufenuron tablets was initiated prior to the flea season, mean flea counts were lower in lufenuron-treated dogs versus placebo-treated dogs. After 6 monthly treatments, the mean number of fleas on lufenuron-treated dogs was approximately 4 compared to 230 on placebo-treated dogs.

When treatment was initiated during the flea season, lufenuron tablets were effective in controlling flea infestations on dogs that completed the study. The mean flea count per lufenuron-treated dog was approximately 74 prior to treatment but had decreased to 4 after six monthly doses of lufenuron. A topical adulticide was used in the first eight weeks of the study to kill the pre-existing adult fleas.

Safety: Milbemycin Oxime

Milbemycin oxime has been tested safely in over 75 different breeds of dogs, including collies, pregnant females, breeding males and females, and puppies over two weeks of age. In well-controlled clinical field studies 786 dogs completed treatment with milbemycin oxime. Milbemycin oxime was used safely in animals receiving frequently used veterinary products such as vaccines, anthelmintics, antibiotics, steroids, flea collars, shampoos and dips.

Two studies in heartworm-infected dogs were conducted which demonstrated mild, transient hypersensitivity reactions in treated dogs with high microfilaremia counts (see Precautions for reactions observed). Safety studies in pregnant dogs demonstrated that high doses (1.5 mg/kg = 3X) of milbemycin oxime given in an exaggerated dosing regimen (daily from mating through weaning), resulted in measurable concentrations of the drug in milk. Puppies nursing these females which received exaggerated dosing regimens demonstrated milbemycin-related effects. These effects were directly attributable to the exaggerated experimental dosing regimen. The product is normally intended for once-a-month administration only. Subsequent studies included using 3X daily from mating to one week before weaning and demonstrated no effects on the pregnant females or their litters. A second study where pregnant females were dosed once at 3X the monthly use rate either before, on the day of or shortly after whelping resulted in no effects on the puppies.

Some nursing puppies, at 2, 4, and 6 weeks of age, given greatly exaggerated oral doses of milbemycin oxime (9.6 mg/kg = 19X) exhibited signs typified by tremors, vocalization and ataxia. These effects were all transient and puppies returned to normal within 24 to 48 hours. No effects were observed in puppies given the recommended dose of milbemycin oxime (0.5 mg/kg). This product has not been tested in dogs less than 2.2 pounds in body weight.

A rising-dose safety study conducted in rough-coated collies manifested a clinical reaction consisting of ataxia, pyrexia and periodic recumbency in one of fourteen dogs treated with milbemycin oxime at 12.5 mg/kg (25X monthly use rate). Prior to receiving the 12.5 mg/kg dose (25X monthly use rate) on day 56 of the study, all animals had undergone an exaggerated dosing regimen consisting of 2.5 mg/kg milbemycin oxime (5X monthly use rate) on day 0, followed by 5.0 mg/kg (10X monthly use rate) on day 14 and 10.0 mg/kg (20X monthly use rate) on day 32. No adverse reactions were observed in any of the collies treated with this regimen up through the 10.0 mg/kg (20X monthly use rate) dose.

Safety: Lufenuron

Lufenuron tablets have been used and tested safely in over forty breeds of dogs, including pregnant females, breeding males and puppies over six weeks of age. In well-controlled clinical trials, 151 dogs completed treatment with lufenuron tablets. Lufenuron tablets were used safely in animals receiving frequently used veterinary products such as vaccines, anthelmintics, antibiotics and steroids. In a ten-month study, doses up to 10X the recommended dose rate of 10 mg/kg caused no overt toxicity. A single dose of 200 mg/kg (20X the recommended dose rate) had no marked effect on adult dogs, but caused decreased activity and appetite in eight week old puppies. Mean body weights of male and female puppies were higher in treated versus control group at the end of the study. In specifically designed target animal safety studies, lufenuron tablets were tested with concurrent administration of flea adulticides containing carbaryl, permethrin, chlorpyriphos and cythioate. No toxicity resulted from these combinations. Lufenuron tablets did not cause cholinesterase inhibition nor did they enhance cholinesterase inhibition caused by exposure to organophosphates.

Four reproductive safety studies were conducted in breeding dogs with lufenuron tablets: two laboratory and two well-controlled clinical studies. In one of the laboratory studies, where lufenuron was administered to beagle dogs at doses equivalent to 90X (3X daily) the monthly recommended dose of 10 mg/kg, the ratio of gravid females to females mated was 8/8 or 100% in the control group and 6/9 or 67% in the lufenuron-treated group. The mean number of pups per litter was two animals higher in the treated versus control groups and the mean birth weights of pups from treated bitches in this study was lower than control groups.

These pups grew at a similar rate to control pups. There was a higher incidence of four clinical signs in the lufenuron-treated versus control group: nasal discharge, pulmonary congestion, diarrhea/dehydration and sluggishness. The incidence of these signs was transient and decreasing by the end of lactation. Results from three additional reproductive safety studies, one laboratory and two clinical field studies evaluating eleven breeds of dogs, did not demonstrate any adverse findings for the reproductive parameters measured including fertility, pup birth weights and pup clinical signs after administration of lufenuron up to 5X the recommended monthly use rate.

Data from analysis of milk from lactating animals treated with lufenuron tablets at 2X and 6X the recommended monthly use rate demonstrates that lufenuron concentrates in the milk of these dogs. The average milk:blood concentration ratio was approximately 60 (i.e., 60X higher drug concentrations in the milk compared to drug levels in the blood of treated bitches). Nursing puppies averaged 8-9 times higher blood concentrations of lufenuron compared to their dams.

Dosage

SENTINEL FLAVOR TABS are given orally, once a month, at the recommended minimum dosage of 0.23 mg/lb (0.5 mg/kg) milbemycin oxime and 4.55 mg/lb (10 mg/kg) lufenuron.

Dogs over 100 lbs are provided the appropriate combination of tablets.

Administration

TO ENSURE ADEQUATE ABSORPTION, ALWAYS ADMINISTER **SENTINEL® FLAVOR TABS®** TO DOGS IMMEDIATELY AFTER OR IN CONJUNCTION WITH A NORMAL MEAL.

SENTINEL FLAVOR TABS are palatable and most dogs will consume the tablet when offered by the owner. As an alternative to direct dosing, the tablets can be hidden in food. Be certain the dog consumes the entire tablet or tablets. Administer SENTINEL FLAVOR TABS to dogs immediately after or in conjunction with a normal meal. Food is essential for adequate absorption of lufenuron. Watch the dog closely following administration to be sure the entire dose has been consumed. If it is not entirely consumed, redose with the full recommended dose as soon as possible.

Recommended Dosage Schedule

Body Weight	Milbemycin Oxime Per Tablet	Lufenuron Per Tablet
2 to 10 lbs.	2.3 mg	46 mg
11 to 25 lbs.	5.75 mg	115 mg
26 to 50 lbs.	11.5 mg	230 mg
51 to 100 lbs.	23 mg	460 mg

SENTINEL FLAVOR TABS must be administered monthly, preferably on the same date each month. Treatment with SENTINEL FLAVOR TABS may begin at any time of year. In geographic areas where mosquitoes and fleas are seasonal, the treatment schedule should begin one month prior to the expected onset and should continue until the end of "mosquito and flea season." In areas with year-round infestations, treatment should continue through the entire year without interruption.

If a dose is missed and a 30-day interval between dosing is exceeded, administer SENTINEL FLAVOR TABS immediately and resume the monthly dosing schedule. If SENTINEL FLAVOR TABS replace daily diethylcarbamazine (DEC) for heartworm prevention, the first dose must be given within 30 days after the last dose of DEC.

Adverse Reactions

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

To report suspected adverse drug events, contact Virbac at 1-800-338-3659. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or http://www.fda.gov/AnimalVeterinary/SafetyHealth.

How Supplied

SENTINEL FLAVOR TABS are available in four tablet sizes (see Dosage Section) formulated according to the weight of the dog. Each tablet size is available in color-coded packages of 6 or 12 tablets each, which are packaged 10 per display carton.

Storage Conditions

Store in a dry place at controlled room temperature, between 59° and 77°F (15-25°C).

Questions? Comments?
Please Call 1-800-338-3659
Visit our website at www.sentinelpet.com

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

NADA #141-084, Approved by FDA

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Virbac

Optimizing Flea Prevention Protocols

Sponsored by Virbac Corporation

Although topical flea preventives can be effective when used properly, owner reluctance or preference for oral preventives are common realities. Lufenuron, an oral flea control product, is a chitin synthesis inhibitor that prevents flea eggs from hatching, prevents larvae from developing, and has revolutionized flea infestation treatment options.

After the initial release of lufenuron, SENTINEL® FLAVOR TABS® (milbemycin oxime/lufenuron) and SENTINEL® SPECTRUM® (milbemycin oxime/lufenuron/praziquantel) were approved by the FDA for [1,2]:

- Prevention and control of flea populations
- Prevention of heartworm disease caused by *Dirofilaria immitis*
- Treatment and control of adult hookworms *(Ancylostoma caninum)*
- Treatment and control of roundworms *(Toxocara canis, Toxascaris leonina)* and whipworms *(Trichuris vulpis)*
- Treatment and control of tapeworms *(Echinococcus multilocularis, Echinococcus granulosus, Taenia pisiformis)**

Picking the Protocol

A protocol must address the individual needs of patients and owners. A potential protocol might look like this:

- SENTINEL FLAVOR TABS
  - Monthly heartworm prevention
  - Insect growth regulator (IGR)-based flea control
- EFFITIX® PLUS Topical Solution for Dogs
  - Monthly
  - Kills fleas and ticks

Depending on clinician and owner preferences, other products can be used. It is important to remember that although these products have well-established safety profiles, there are no studies documenting the safety of concurrent use of these products.

If fleas are only eliminated at one point in the life cycle, then lapses in compliance may make the cycle easier to reestablish. Including the IGR in these newer protocols may offer more robust flea control.

Important Safety Information for SENTINEL FLAVOR TABS: Dogs should be tested for heartworm infection prior to use. In a small percentage of treated dogs, digestive, neurologic, and skin side effects may occur. For complete product information, refer to the product insert. To obtain a product insert, contact Veterinary Technical Product Support at 1-800-338-3659, or visit us.virbac.com.

Important Safety Information for SENTINEL SPECTRUM: Dogs should be tested for heartworm infection prior to use. Mild hypersensitivity reactions have been noted in some dogs carrying a high number of circulating microfilariae. Treatment with fewer than 6 monthly doses after the last exposure to mosquitoes may not provide complete heartworm prevention. For complete product information, refer to the product insert. To obtain a product insert, contact Veterinary Technical Product Support at 1-800-338-3659, or visit us.virbac.com.

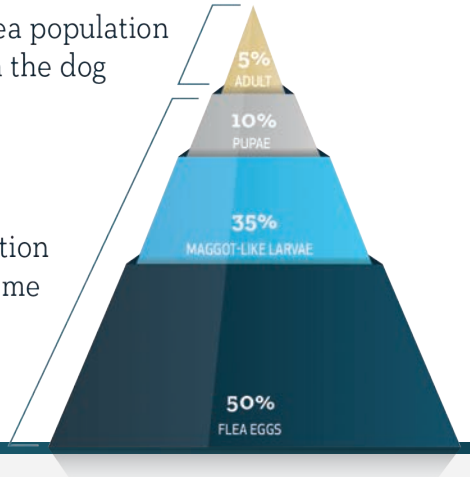
Important Safety Information for EFFITIX PLUS Topical Solution for Dogs: For use only on dogs and puppies 8 weeks of age or older weighing at least 5 lbs.
DO NOT USE ON CATS.

FLEA LIFE CYCLE: KEY POINTS[3]

- Composition of flea populations is estimated to be 5% adult fleas, 50% flea eggs, 35% flea larvae, and 10% pupae
- One adult flea can lay thousands of eggs
- Maggot-like flea larvae migrate away from light and into carpet and cracks in flooring, where they can remain active in the environment
- Pupal development is highly dependent on warm, humid conditions
- Once emerged, adult fleas feed and breed quickly

5% of the flea population develops on the dog

95% of the flea population develops inside the home



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*Applies only to SENTINEL SPECTRUM.

See page 22 for product information summary.

Feline Heart Disease

Heart disease should be suspected in cats with a heart murmur, gallop, or arrhythmia and should be considered in cats over 9 years of age. In patients presented with these signs, hyperthyroid disease, anemia, and hypertension should be ruled out. Most cats at high risk for congestive heart failure (CHF) or arterial thromboembolism (ATE) have left atrial dilation; with practice, clinicians should be able to identify enlarged left atria on ultrasonography. Point-of-care N-terminal probrain natriuretic peptide (NT-proBNP) can be a useful screening test, although false negatives can occur. NT-proBNP is better at identifying high-risk heart disease than it is mild heart disease. In cats presented in respiratory distress, a positive NT-proBNP test result can be particularly helpful in determining if CHF is the cause of respiratory distress.

Cats with grade 5 or 6 heart murmurs are likely to have congenital heart disease, and referral should be offered. Other cases for which referral might be considered include cats with a gallop rhythm, arrhythmia, elevated NT-proBNP concentration, and clinical signs such as open-mouth breathing or syncope. Cats being treated for CHF that respond poorly to treatment should also be referred. Cats with preclinical disease may be monitored with a combination of echocardiography (to watch for left atrial dilation) and NT-proBNP concentrations. Cats with a history of heart failure or ATE can be monitored at home via measurement of the resting or sleeping respiratory rate.—*Fuentes VL*

Proliferation Markers & Immunohistochemistry

Immunohistochemistry detects specific binding of antibodies to their specific tissue antigens and can be used for definitive diagnosis and subclassification of neoplasms through identification of cells of origin. Because tissue antigen expression is heterogeneous, a panel of antisera rather than a single marker is required, complicating interpretation of staining profiles.

In addition to diagnostic information, immunohistochemistry can also be used for prognostic purposes, as different markers of cell proliferation can identify cells in various stages of the cell cycle. One such marker is Ki67, a protein essential in cell cycle progression. The Ki67 staining index is used for predicting prognosis of canine mast cell tumors and melanocytic tumors; these are the only tumors for which specific cut-off values have been identified for predicting prognosis. Silver staining of nucleolar organizer regions (AgNOR) enables assessment of cell cycle time. In patients with canine mast cell tumors, lower scores are associated with longer survival times; however, the AgNOR score does not provide additional prognostic information than that already provided by the Patnaik grading system.

Immunohistochemistry can also be used for analysis of potential therapeutic targets in neoplastic tissues. For example, c-Kit (CD117) is expressed by mast cell tumors and all GI stromal tumors and is a potential target for the receptor tyrosine kinase antagonists toceranib and masitinib.—*Scase T*

Imaging of the Head

Although MRI and CT are being used increasingly in the investigation of diseases of the head, their availability is limited and their cost is high; thus, radiography remains an important diagnostic tool in veterinary medicine. Sedation and anesthesia are important for proper positioning, as multiple projections are often necessary.

When investigating the nasopharynx, dorsoventral and lateral views, as well as dorsoventral intraoral (ie, ventrorostral-caudodorsal oblique open-mouth) projections, can help maximize visualization of the nasal chambers. Because many nasal diseases extend into the sinuses, a skyline view of the frontal sinuses is recommended. Normal nasal turbinates should appear bilaterally symmetrical. Blurring or destruction of the turbinates may indicate disease, as can changes in opacity of surrounding tissues. Loss of normal detail in the nasopharynx can indicate a mass effect or its structural opposite, stenosis.

When visualizing the tympanic bullae, positioning is crucial so as to limit artifacts. In dogs, a rostrocaudal open-mouth view is best, whereas in cats, the mouth can remain closed, and a rostral 10-degree ventral-caudodorsal oblique view should be obtained. Otitis media can result in subtle increased opacity of the bullae. Chronic disease can result in thickening of the bulla wall. More severe disease or neoplasia may result in wall thinning or obliteration. Mineralization of the outer ear canal wall may be noted with chronic otitis externa.

Radiography can also be helpful when looking for fractures or neoplasia in the mandible and maxilla.—*Hammond G*

Psychoactive Drugs

In veterinary medicine, psychoactive drugs may be used for the treatment of anxiety and phobias as well as for the management of neurochemical disorders (eg, compulsive behaviors, cognitive dysfunction). Psychoactive drugs work by altering activity of certain neurotransmitters in the brain, including monoamines (ie, serotonin, dopamine, norepinephrine) and γ-aminobutyric acid. Behavioral drugs only modulate—rather than change—behaviors and should not substitute proper behavior modification therapy.

- Selective serotonin reuptake inhibitors raise serotonin levels and are used to control reactivity, reduce anxiety, and improve responsiveness to training.
- Tricyclic antidepressants block reuptake of serotonin and, to a lesser extent, norepinephrine. Their anticholinergic and antihistaminic properties are responsible for side effects such as sedation and urine and stool retention.
- Benzodiazepines potentiate γ-aminobutyric acid effects, resulting in decreased anxiety, hyperphagia, and muscle relaxation. They have a quick onset and short duration of action in dogs and are primarily used on an as-needed basis.
- β blockers and α_2 agonists can reduce the physiologic signs of anxiety (eg, heart rate, respiratory rate) and are likely best used in combination with drugs that decrease behavioral anxiety.
- Anticonvulsants may be considered in patients with temporal lobe or generalized seizures that cause mood alterations or hallucinatory or self-traumatic behaviors.

Psychoactive drugs must be selected carefully and slowly titrated to effect. Many take 1 to 3 weeks to begin working and even longer to reach maximal efficacy. Trial and error may be necessary to find the right psychoactive drug for an individual patient.—*Denenberg S*

Psychoactive drugs must be selected carefully and slowly titrated to effect.

Managing Dogs with Gastrointestinal Disorders:

The Skinny on Dietary Fat and Nutrient Absorption

Arleigh Reynolds, DVM, PhD, DACVN
Senior Research Scientist
Nestlé Purina PetCare

Associate Professor of Veterinary Nutrition
Associate Dean, Department of Veterinary Medicine
University of Alaska Fairbanks

When a dog presents with diarrhea, one of the first steps is to distinguish between small and large bowel diarrhea. What are the primary steps in diagnosis?

Fecal examination is the first step. Small bowel diarrhea generally presents with large volumes of stool, which look like fairly undigested material, including fat globules. Large bowel diarrhea presents with small, frequent bouts of diarrhea, often with mucus and sometimes with frank blood. Parasites in the feces can cause problems in either the large or small bowel.

Blood work can also tell us a lot, especially when small bowel diarrhea is suspected:

- A CBC can indicate infection or inflammation.
- Changes in plasma values may warrant further testing to check for alterations in cobalamin or folate levels.
- Maldigestion may suggest a need to evaluate pancreatic or brush border enzymes.

Regardless of the cause, how do GI conditions affect a dog's ability to digest and absorb nutrients?

Whenever there is a disturbance in GI function, there's a decreased ability to digest and absorb nutrients from food. In the small bowel, digestion occurs with pancreatic enzymes, which do the initial work of digestion; whereas the brush border enzymes complete digestion, particularly of carbohydrates. Any disease that affects either the rate of passage of food through the small intestine or disturbs the mucosal surface and therefore affects the brush border enzymes is going to affect digestion.

Additionally, anything that affects the surface of the intestinal tract is going to affect absorption. That's particularly true with fat, because it's probably the most complicated nutrient in the way it's digested and absorbed.

What characteristics should you look for in a GI diet? Are some fats and carbohydrates more digestible than others?

Most fats we feed are long-chain fatty acids, which a healthy animal can digest and absorb just fine. However, if a dog has diarrhea, we may switch to a lower-fat diet and/or a diet with medium-chain triglycerides which are more easily digestible (although there is a limit to the amount of these that can be fed) to help ease the burden on the enterocytes — the cells that line the intestinal tract — as they process fat.

Carbohydrates can be complex in their structure, and the way different carbohydrates bond together and how they're processed also affect digestibility. For example, raw starches aren't very digestible, but if they are cooked properly they can become highly digestible.

Is fat restriction always the answer for dogs with GI disorders? When is a low-fat diet recommended for GI patients, and when isn't it?

Restricting fat is unnecessary for a large-bowel problem such as colitis. Fat intake should be decreased in any condition with compromised bile or pancreatic secretion, or abnormal enterocyte function. If it's not, nutrients will not be properly digested and will end up in the large bowel, which will exacerbate the amount of bacterial growth and cause diarrhea.

For small bowel disorders such as dietary indiscretion, infection or inflammation, it may be necessary to restrict fat in the initial stages until we can get the underlying cause under control. After that, we can gradually return the patient to a diet that's higher in fat with more complex carbohydrates.

Diagnosing Diarrhea

Step 1. Fecal Examination

LARGE BOWEL
Small, frequent bouts of diarrhea possibly with mucus and/or frank blood

SMALL BOWEL
Large volume of stool with undigested material, including fat globules

Step 2. Blood Tests

- I.D. infection or inflammation
- Changes in plasma values that suggest vitamin deficiencies
- Evaluate pancreatic and brush border enzymes

GI Nutrition: Match the Diet to the Issue

Deborah Greco, DVM, PhD, DACVIM
Senior Research Scientist
Nestlé Purina PetCare

Determining the cause of acute and chronic gastrointestinal (GI) symptoms is essential to formulating a management plan; once diagnosed, different disorders call for different forms and levels of fat, carbohydrate, fiber and other nutrients. Following is an overview of dietary characteristics to consider when recommending a GI diet.

GI Diet With Moderate Fat and High Total Digestibility

DIET PROFILE: Diet contains moderate levels of fat and calories, with easily digested type of fat, like medium-chain triglycerides (MCTs); a prebiotic; and added nutrients such as omega-3 fatty acids and bovine colostrum.

GI INDICATIONS: Small bowel GI disorders, including gastritis and enteritis; vomiting and diarrhea; malabsorption and maldigestion; exocrine pancreatic insufficiency.

RATIONALE: Dogs with a wide range of small bowel GI disorders benefit from a diet with a highly digestible fat that can be readily utilized as an energy source, as well as prebiotic fiber that helps nourish a healthy GI tract.

GI Diet With Fiber

DIET PROFILE: Diet contains optimal levels of fiber (soluble and insoluble), moderate levels of fat and calories, complex carbohydrates and a prebiotic.

GI INDICATIONS: Fiber responsive colitis, constipation, large bowel diarrhea.

RATIONALE: Dogs with large bowel diarrhea and constipation do not require a low-fat diet, but they do respond to optimal levels of fiber that promote intestinal motility. Nutrients that support a healthy digestive tract are also important.

Low-Fat GI Diet With High Total Digestibility

DIET PROFILE: Diet with high total digestibility and a prebiotic, specifically formulated to be low in fat.

INDICATIONS: Pancreatitis, lymphangiectasia, hyperlipidemia.

RATIONALE: Dogs with GI conditions that cause difficulty digesting fat should be fed a low-fat diet that has a high total digestibility to promote nutrient absorption and is formulated with prebiotic that helps nourish a healthy GI tract.

Hydrolyzed Diet

DIET PROFILE: Highly digestible diet contains hydrolyzed protein from a soy protein source with a low molecular weight; contains medium-chain triglycerides; and a single, low-allergen carbohydrate source.

GI INDICATIONS: Food allergy, inflammatory bowel disease.

RATIONALE: Dogs with gastroenteritis from food allergy and/or inflammatory bowel disease benefit from a diet with hydrolyzed proteins and a single, low-allergen carbohydrate source to avert immune response.

What are the benefits of bovine colostrum in a GI diet?

Deborah Greco, DVM, PhD, DACVIM
Senior Research Scientist, Nestlé Purina PetCare

Bovine colostrum is rich in immunoglobulins and other bioactive growth factors that benefit GI health and provide a favorable environment for beneficial bacteria. Nestlé Purina research has shown that dietary supplementation with colostrum may benefit dogs with GI issues.

In a 40-week study of 24 sled dogs between the ages of 2 and 7,[1] dogs were fed either a control diet or a control diet supplemented with bovine colostrum. Throughout the study, in which dogs underwent exercise stress, both gut and immune health were monitored. The results demonstrated:

- Dogs fed the colostrum-supplemented diet had increased intestinal microflora diversity, which may reduce the opportunity for bacterial pathogens.
- Colostrum-fed dogs had more stable microbial populations following exercise challenge, which helped reduce the risk of stress-related diarrhea.

GI Screening: Diagnosis Starts With Discussion

Karen Poteete, DVM
Kare Bears Cuddly Paws
Polk County, Georgia

While GI issues are a common problem in my canine patients, owners often are unaware that their pets are affected. Vomiting and diarrhea are either considered "normal" or assumed to be phases that will pass on their own. Often, it isn't until the dog actually stops eating that the problem is brought to my attention.

The first step is to learn the pet's history—something that may be easier said than done. Successfully screening for GI issues entails not just asking "yes" or "no" questions, but asking open-ended questions that encourage owners to provide as many details as possible about their pet's condition.

A client recently called me in a panic a few days after I had vaccinated his puppies. They had become lethargic and he was convinced it was due to the vaccine. Upon probing, I learned that some of the puppies had diarrhea and there were soft stools in the yard. A fecal test revealed that the real culprit was giardia.

"Show and tell" facilitates diagnosis, compliance

Rather than asking if a dog's stool is normal, I ask the owner to describe the stool, and follow with questions such as "How frequently does she poop?" and "Is she having any difficulty?" I often use the Purina fecal scoring chart to show owners what a healthy stool looks like. It helps them understand the importance of their pet's GI health and may — as in the case of the vaccinated puppies — help uncover information that leads to a diagnosis.

- Fecal IgA levels, which indicated enhanced local immune status, were higher in colostrum-fed dogs.
- Colostrum-fed dogs maintained higher antibody titers against canine distemper virus from 16 weeks post-vaccination through the end of the trial (40 weeks) than dogs fed the control diet.

1 *Satyaraj E, Reynolds A, Pelker R, et al. Supplementation of diets with bovine colostrum influences immune function in dogs. Brit J of Nutr. June 2013.*

Successfully screening for GI issues entails not just asking "yes" or "no" questions but asking open-ended questions that encourage owners to provide as many details as possible.

Once a dog's GI condition is diagnosed, explaining exactly why I'm recommending a specific course of action can get clients past compliance hurdles. Personal stories also help, and I'm quick to reassure owners that I don't recommend anything I wouldn't do for my own dog. If a client is hesitant or expresses concern that his or her dog won't eat a prescription diet, I open a can of the food I'm recommending and feed it to the dog right in the office. Not only does this demonstrate my trust in the product, it also reassures the client that the dog will find the diet palatable.

In most cases, I follow up with clients approximately one week into treatment, at which time I expect their dog to be making significant progress. In the case of the puppies with giardia, a combination of metronidazole and a diet of Purina® Pro Plan® Veterinary Diets EN Gastroenteric® Canine formula eliminated the diarrhea in a short period of time.

Diet is always an important component of my recommendations for pets with GI problems, because they are both effective and compliance-friendly. Even clients who are slow to acknowledge a GI problem or who have trouble sticking to a dosage schedule can follow a nutritional management plan. All they have to do is feed their dog.

Key Takeaways

- If a dog has diarrhea, it may be prudent to switch to a lower-fat diet and/or a diet with medium-chain triglycerides (though there is a limit to the amount of MCTs that can be fed) to help ease the burden on the intestinal tract as it processes fat.
- GI diets for dogs are not one-size-fits-all. Depending on their condition, dogs may benefit from different levels — and types — of fat, carbohydrate and fiber, as well as added nutrients like antioxidants, prebiotics and colostrum.
- When screening patients for GI issues, ask open-ended questions and take the time to educate clients about GI health to help reach a diagnosis.

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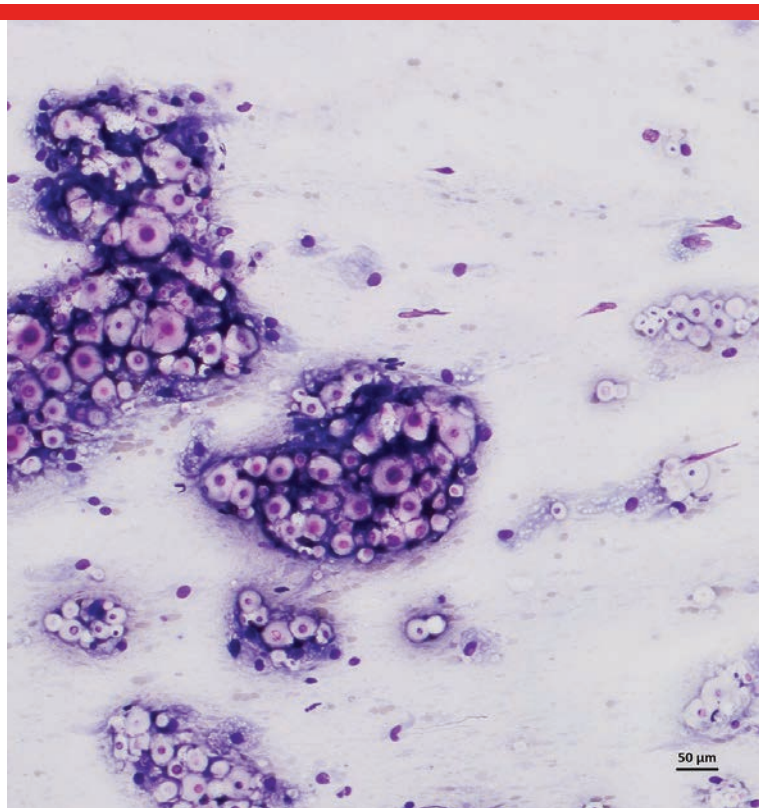
**Conclusion based in part on Kynetec 2017 Veterinary Landscape Canine Gastrointestinal Cases – diagnosis as percent of GI cases*

Lameness & Osteomyelitis in a Cat



Lauren Chapman, DVM
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Adelaide, Australia

History

A skeletally mature (age unknown), 8.6-lb (3.9-kg) spayed domestic shorthair cat was evaluated for acutely worsening left pelvic limb lameness. Mild lameness had been observed for approximately 4 weeks before presentation. The patient was not receiving any medications and had been adopted in New Mexico 4 years prior. The owner reported no travel history since adoption; however, limited prior medical records indicated that the patient had been vaccinated in Northern California prior to adoption.

Physical Examination

The principal physical examination finding was a firm, painful, circumferential swelling of the left proximal metatarsal/tarsal region accompanied by a nonweight-bearing lameness on that limb. The remainder of the physical examination was unremarkable. Rectal temperature was 101.8ºF (38.8ºC), heart rate was 200 bpm, and respiratory rate was 36 breaths/min with no increased respiratory effort observed.

Diagnostics

Serum chemistry profile, urinalysis, and CBC were unremarkable, and the patient was negative for FIV antibodies and FeLV antigen.

Radiographs of the left proximal metatarsal/tarsal region revealed multiple foci of osteolysis within the distal tarsal and proximal metatarsal bones, as well as marked soft tissue swelling of the area (***Figure 1***). Periosteal reaction was noted on the dorsal and plantar surfaces of the distal tarsal and proximal metatarsal bones.

Radiographs of the thorax revealed a diffuse, finely granular interstitial pulmonary infiltrate with prominent bronchial markings with indistinct nodules in the middle and caudal lung lobes (***Figure 2***).

A fine-needle aspirate was collected from the proximal metatarsal/tarsal swelling (***Figure 3***, page 28). Cytologic evaluation revealed a granulomatous inflammatory infil-

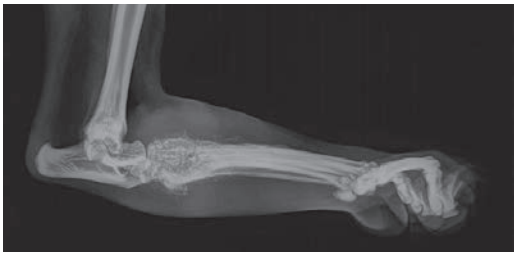
trate and abundant capsulated yeast organisms demonstrating occasional narrow-based budding. The morphology of these organisms was consistent with *Cryptococcus* spp infection.

A *Cryptococcus* spp antigen agglutination test was positive (titer 1:3688). Because of the uncommon presentation of fungal osteomyelitis, biopsies of the tarsal swelling were submitted for histopathologic analysis and fungal identification by genetic sequencing. Histopathologic analysis confirmed the organisms were consistent with *Cryptococcus* spp and described severe, focally extensive, granulomatous osteomyelitis and cellulitis with intralesional encapsulated yeast organisms. DNA-based analysis matched that of *Cryptococcus gattii* type V, molecular type VGIII.

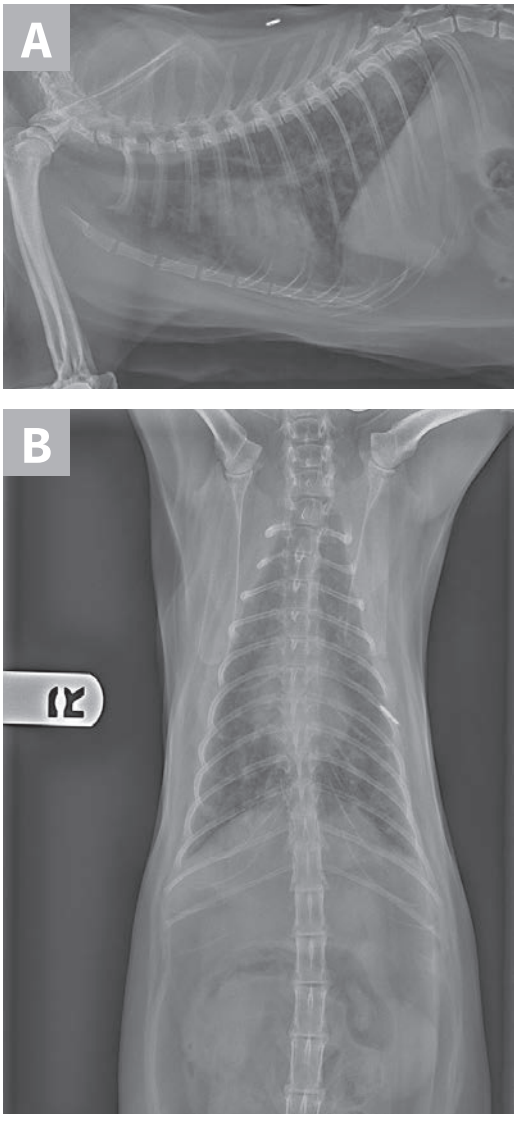
Treatment & Outcome

Treatment was initiated with fluconazole (12.8 mg/kg PO q12h) and buprenorphine (0.015 mg/kg transmucosal q8h) for pain.[1,2] Fluconazole was used for about one month. Following a discussion with a veterinary mycosis specialist, treatment was changed to itraconazole (12.8 mg/kg PO q12h; later reduced to 9 mg/kg PO q12h) and amphotericin B (0.55 mg/kg as a diluted [in 350 mL of 0.45% NaCl with 2.5% dextrose] twice-weekly SC infusion) based on the results of diagnostic testing that further classified the *Cryptococcus* spp strain.

Clinical signs resolved within 2 months and did not return. A total of 20 doses of amphotericin B were administered to reach a cumulative dose of approximately 10 mg/kg. Hepatic and renal parameters were monitored. Renal values remained within the reference interval, but a mildly elevated alanine aminotransferase persisted (162-249 U/L; reference range, 10-100 U/L). Based on intolerance (ie, inappetance, vomiting) to the initial dose of itraconazole, the dose was reduced to 8.5 mg/kg PO q12h, and treatment was continued for approximately 2 years after initiating therapy until the patient was seronegative on 2 occasions one month apart. At the final follow-up, the patient appeared healthy with no signs of illness. Lengthy, possibly lifelong, treatment may be required for some patients.[3] Even when clinical signs resolve, relapse is still possible.[4] A better prognosis has been observed in animals treated



▲ **FIGURE 1** Multiple foci of osteolysis and surrounding marked soft tissue swelling in the distal tarsal and proximal metatarsal bones



▲ **FIGURE 2** Diffuse, finely granular interstitial pulmonary infiltrate (***A***) with prominent bronchial markings with indistinct nodules in the middle and caudal lung lobes (***B***)

early or those with only localized disease without CNS or systemic involvement.[5]

Discussion

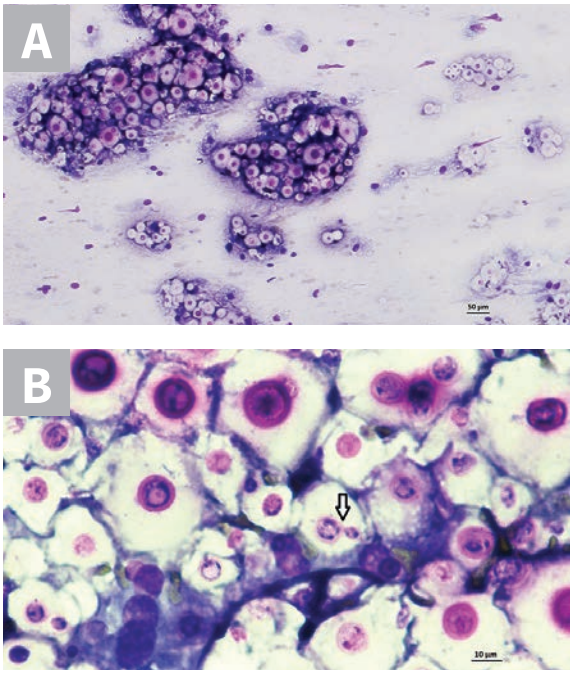
C gattii was long considered an organism of tropical and subtropical climates. However, *C gattii*-endemic areas now include western Canada and the Pacific Northwest region of the United States.[6]

Unlike infection with other *Cryptococcus* spp organisms, *Cryptococcus gattii* infection tends to occur in immunocompetent individuals.[3] In cats, infection typically occurs after basidiospore entry into the patient from the environment via inhalation and colonization of the nasal cavity, followed by tissue invasion of structures in the sinonasal cavity. Extension occasionally occurs into the CNS, oral cavity, and/or orbit by penetration of bones surrounding the sinonasal cavity.

This patient's presentation is more consistent with human infection, in which the lung is typically the primary site of infection, with subsequent hematogenous dissemination to brain, bone, skin, and/or other tissues.[6] *C gattii* is not considered to be zoonotic, except in immunocompromised humans.[4] Rather, humans and animals acquire the organisms from the same environmental sources. Animals may serve as important sentinels, which indicates the potential for human exposure from the environment.[5] The incubation period between exposure and clinical signs is variable and reported to be 1 to 12 months or longer.[5]

Young to middle-aged cats are most often diagnosed with cryptococcosis, but all ages can be affected.[4] Distinguishing among species of *Cryptococcus* has become important in epidemiologic studies, but there is no difference between the clinical presentations of infections caused by different members of the *C neoformans/gattii* species complex.[4]

Cats are reportedly 6 times more likely than dogs and 3 times more likely than horses to become clinically affected.[4] Lesions are most often noted in the nasal, maxillary, or frontal regions of the head.[3] Fungal granulomas or lesions involving the lymph nodes and skin of the head and neck are common.[5] CNS and/or ocular involvement is suspected if blindness, retinal (chorioretinitis), or optic disc lesions accompany a diagnosis.[4] Almost any organ system, including the lungs, kidneys, bone, and periarticular tissues, can be affected.[4] Treatment typically consists of antifungal therapy, with close monitoring of liver and renal values.



▲ **FIGURE 3** Cytology of the fine-needle aspirate from swollen tarsus with numerous *Cryptococcus* spp yeast organisms featuring thick clear capsules (***A***). Narrow-based budding is displayed by some of the organisms (***B***; ***arrow***). *100× and 500× magnification, Wright-Giemsa*

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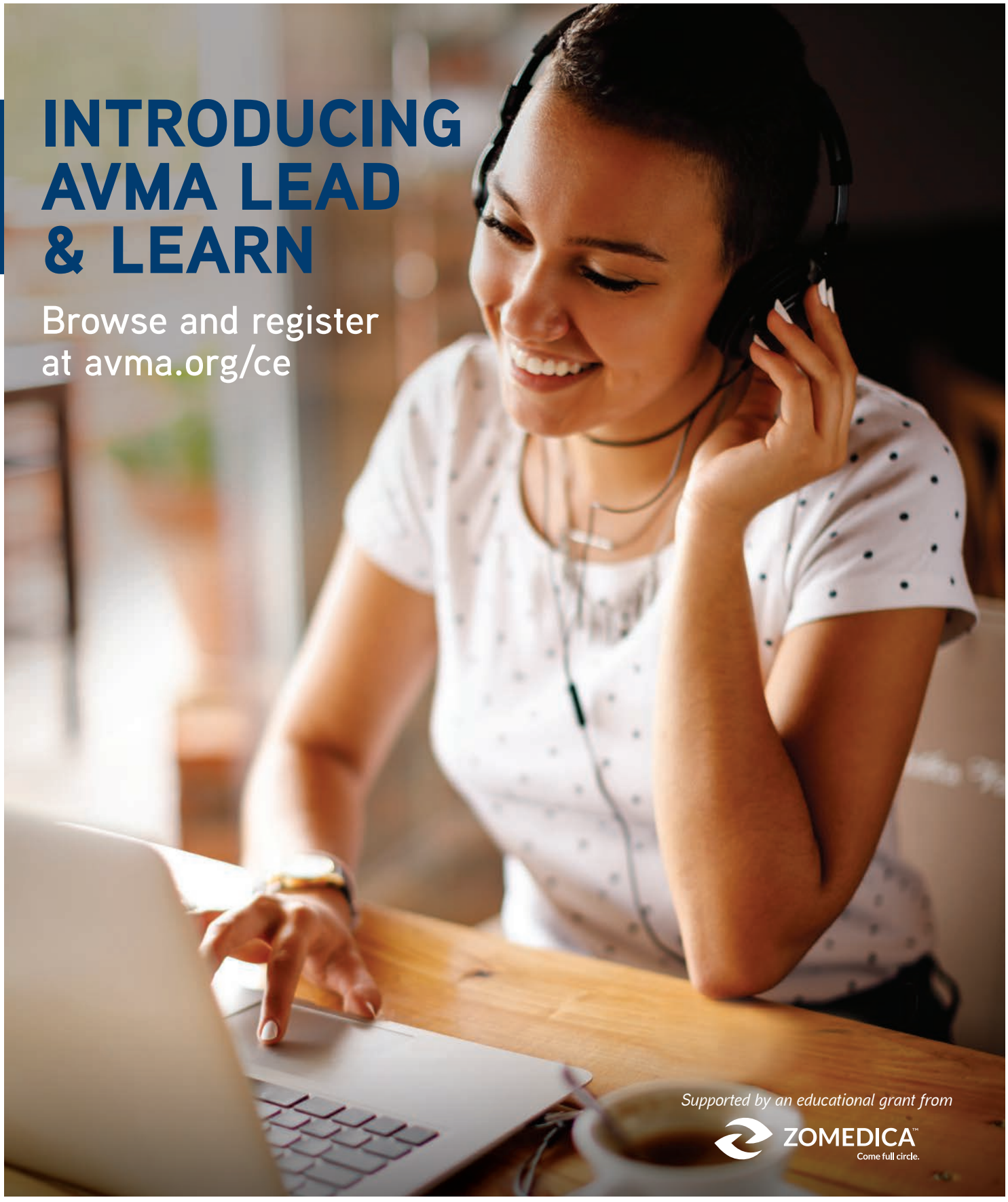

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Fungal Cultures

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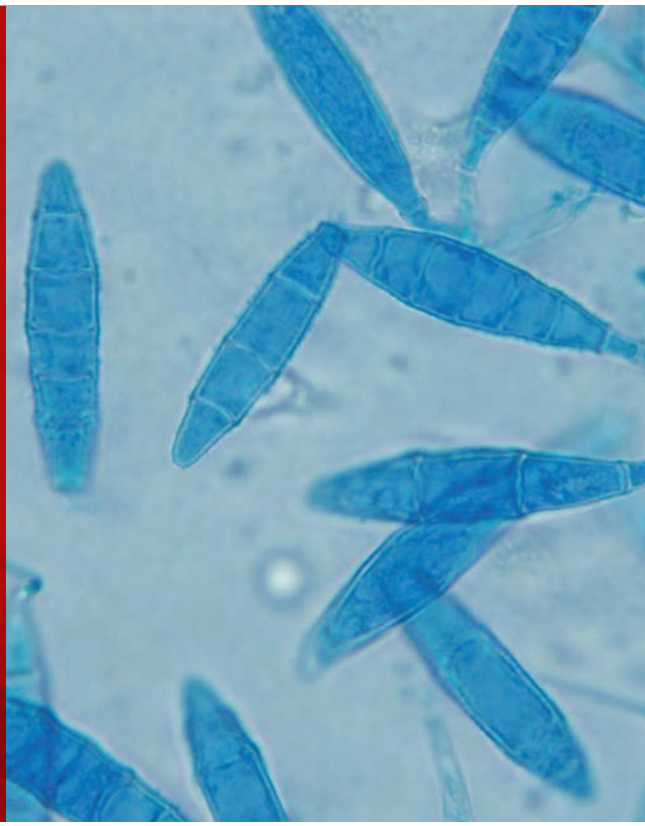


Fungal cultures are an important diagnostic tool that can be easily performed in a general practice setting.[1-3] It is essential to include dermatophytosis in the differential diagnoses for patients with clinical signs consistent with fungal skin infection (eg, multifocal patchy alopecia, crusts, scales, pustules, papules), as well as for patients with similar clinical signs (ie, demodicosis, pyoderma) that fail to respond to appropriate therapy.[1-7] Yorkshire terriers, working dogs, hunting dogs, and Persian cats may be predisposed to dermatophytosis.[3,4,7]

Sample collection for fungal cultures typically involves a hair pluck, which is best performed at lesional margins,[1-4,7] or a sterile toothbrush.[1,2,4,6,7] A sterile toothbrush is recommended for cats and to detect subclinical carriers that lack obvious lesions (eg, cats passively carrying infectious fungal elements that pose a risk to human health and environmental contamination).[1-4,6] Any commercial toothbrush in its original packaging is considered mycologically sterile for this use.

Flat culture plates represent the best medium to use, ideally when divided into 2 compartments: dermatophyte test medium, which selects for dermatophytes, and Sabouraud dextrose agar, which encourages sporulation and thus facilitates identification via microscopy.[1,2,4,7] The shape of other collection containers (eg, jars, tubes) can make inoculation of organisms challenging. In addition, these

containers have tight-fitting lids that can encourage bacterial growth by trapping moisture,[1,2,4] and obtaining samples from these containers to identify fungal macroconidia can be difficult.[4]

Dermatophytes grow best in media slightly above room temperature (ie, 75ºF-86ºF [24ºC-30ºC]).[1-4,7] Ultraviolet light and low humidity prevent growth on culture media.[1,2,4] Cultures should be kept in a dark drawer or cabinet with a small dish of water nearby.[4] Most dermatophytes grow within 2 to 7 days; however, culture plates should be kept for 21 days in case slow-growing variants (eg, *Trichophyton* spp) are present or if antifungal therapy was initiated prior to sampling.[1-3]

Although certain culture media are selective for dermatophytes, contaminant saprophytes can develop and be mistaken for dermatophytes.[1,2,4,5,7] Colony morphology, media color change, and microscopic morphology are the best indicators to differentiate pathogens from contaminants.[1-4] Dermatophyte colonies are white-to-pale in color and fluffy in appearance; saprophytes are often pigmented.[1-3] Color change is caused by a pH indicator within the medium that modifies the color during protein metabolism.[1,2,4] Because dermatophytes prefer protein (eg, keratin), a color change to red should correspond with colony growth consistent with the expected pathogen.[1,2,4] Saprophytes prefer carbohydrates and only use protein if carbohydrates are depleted[1,2,4]; therefore, color change can still occur, but not alongside initial colony growth.[4] Daily observation during prolonged incubation (ie, >10 days) is imperative because saprophytic fungi will eventually cause the distinctive color change to red.[1,2,4]

The most common dermatophytes that infect small companion animals are *Microsporum canis*, *Microsporum gypseum*, and *Trichophyton mentagrophytes*.[1-3,5,6]

Microscopic evaluation of macroconidia is the definitive technique for confirming dermatophytosis.[4] There is a high likelihood of misdiagnosis if microscopy and macroscopic characteristics are not considered.[7] The most common dermatophytes that infect small companion animals are *Microsporum canis*, *Microsporum gypseum*, and *Trichophyton mentagrophytes*.[1-3,5,6]

PCR is currently being investigated as a means of diagnosing dermatophytosis, with results available in 1 to 3 business days versus the 1 to 3 weeks required for final dermatophyte culture results; panels include more than one dermatophyte species and demonstrate high sensitivity and high specificity.[5] Research into the value of PCR as a sole diagnostic tool is ongoing, and fungal culture is still considered the gold standard.

STEP-BY-STEP FUNGAL CULTURES[1-4,7]

STEP 1

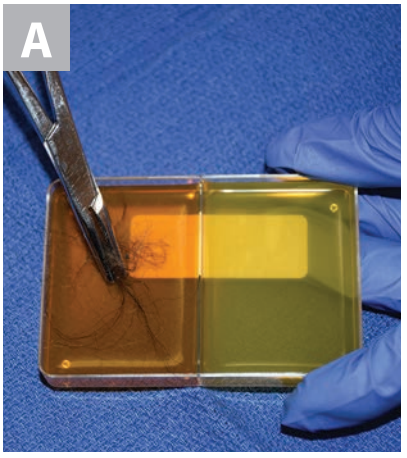
Use a sterile hemostat (ie, hair pluck) or a new sterile toothbrush to obtain culture samples.

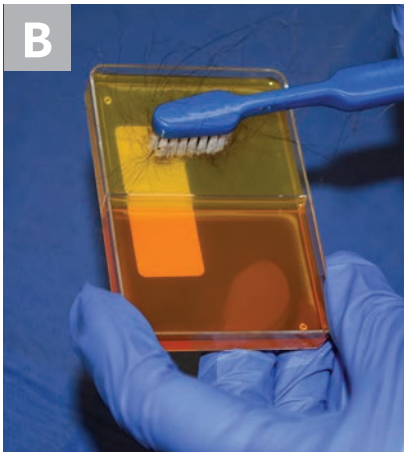
Hair-Pluck Technique (Recommended in Animals with Active Lesions)

Using a sterile hemostat, pluck hairs (≈10-20) from the periphery of lesional skin; the hair bulb and root must be intact. Gently place plucked hair on the culture medium. Ensure the plucked hair remains in place and in contact with the agar by applying gentle pressure with the sterile hemostat (***A***).

Toothbrush Technique (Recommended in Cats & Animals without Obvious Lesions)

Brush a sterile toothbrush through the animal's hair coat, against the direction of growth, for approximately 30 strokes. Lightly press the bristles onto the culture medium (***B***).





WHAT YOU WILL NEED

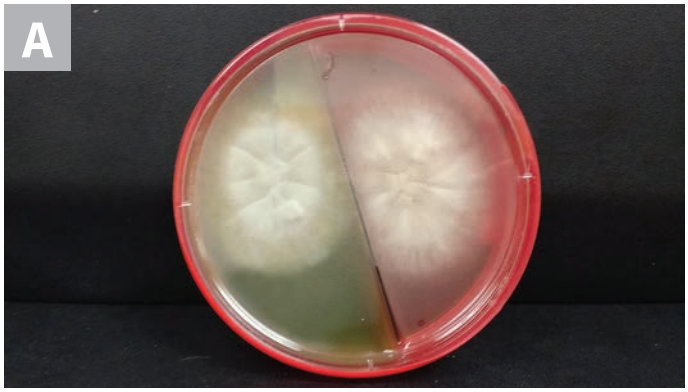
- Sterile hemostat (ie, hair pluck) or new sterile toothbrush
- Divided dermatophyte test medium or Sabouraud dextrose agar plate
- Warm (ie, 75°F-86°F [24°C-30°C]), dark area
- Small dish of water
- Clear acetate tape
- Lactophenol cotton blue or new methylene blue stain
- Light microscope

Author Insight

Broken or misshapen hair and/or hair from inflamed, scaled, or crusted areas are preferred for sampling. Avoid areas that have been recently medicated.

STEP 2

Incubate the closed culture plate in a warm (ie, 75ºF-86ºF [24ºC-30ºC]), dark area for 21 days. Place a small dish of water nearby to provide humidity and prevent the medium from drying out. Check the medium daily for fungal growth.

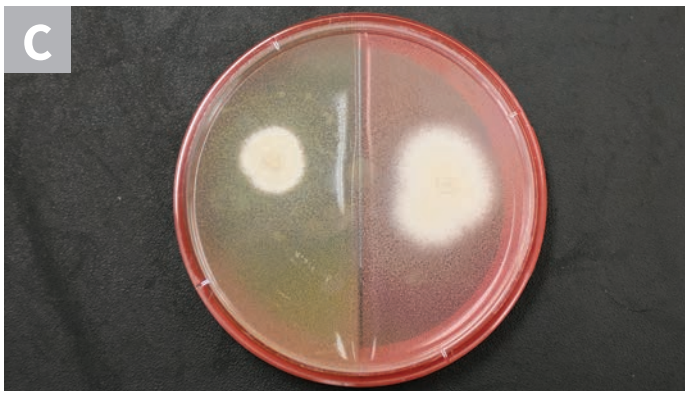


▲ Grossly, colonies of *M canis* are typically white with a cotton-like texture. As they age, they can become powdery and develop a centrally depressed area with radial folds (***A***; colony on split dermatophyte test medium and Sabouraud dextrose agar plate).

Author Insight

Contaminant fungi can cause color change, usually after prolonged incubation (ie, >10 days). Correct interpretation happens when a red color change occurs simultaneously with colony growth; however, making a premature diagnosis based on color change alone can lead to misdiagnosis and unnecessary treatment and potentially delay the ability to render a definitive diagnosis.

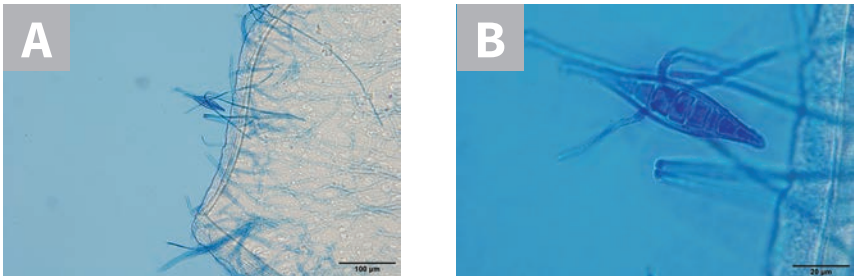
▲ *M gypseum* appears pale-to-light-brown with a flat-to-granular texture. White mycelia can also form (***B***; colony on split dermatophyte test medium and Sabouraud dextrose agar plate).



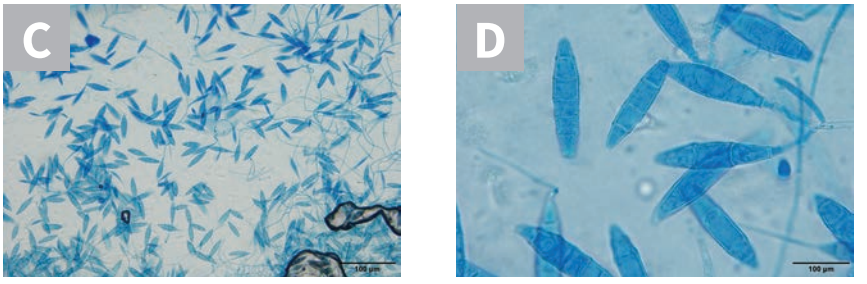
▲ The colony morphology of *T mentagrophytes* is variable. Most zoophilic forms will be white to cream in color with a powdered appearance, whereas the anthrophilic forms typically appear white with a cotton-like texture (***C***; colony on split dermatophyte test medium and Sabouraud dextrose agar plate).

STEP 3

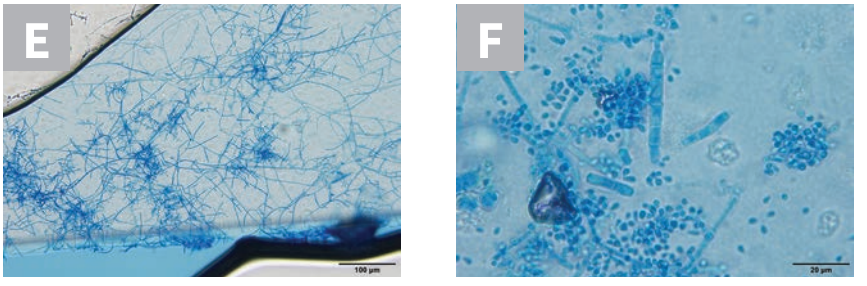
Identify growth on the culture to rule out erroneous results. While wearing gloves, collect macroconidia by gently applying the sticky side of a piece of clear acetate tape to the top of the colony. Place several drops of lactophenol cotton blue stain (as used in the samples shown) or new methylene blue stain on a microscope slide, then place the tape, sticky side down, over it. After placing a coverslip on top, evaluate the sample under the microscope. Alternatively, the entire culture plate can be sent to a diagnostic or commercial laboratory for dermatophyte identification.



▲ *M canis* forms spindle-shaped macroconidia with thick walls and a knob at the terminal end; 6 or more cells per macroconidia are present (***A***, 20×; ***B***, 100× oil immersion).



▲ *M gypseum* forms spindle-shaped macroconidia with thin walls and lacks a knob at the terminal end; 6 or fewer cells per macroconidia will be present (***C***, 20×; ***D***, 100× oil immersion).



▲ *T mentagrophytes* macroconidia are often cigar-shaped with thin walls; some isolates will have spiral hyphae. Globoid microconidia arranged singly or in clusters along hyphae can also be seen (***E***, 20×; ***F***, 100× oil immersion).

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Atypical Hypoadrenocorticism in Dogs

Andrew C. Bugbee, DVM, DACVIM
University of Georgia

In the Literature

Wakayama JA, Furrow E, Merkel LK, Armstrong PJ. A retrospective study of dogs with atypical hypoadrenocorticism: a diagnostic cut-off or continuum? *J Small Anim Pract*. 2017;58(7):365-371.

FROM THE PAGE ...

Atypical hypoadrenocorticism (AH) is an uncommon veterinary endocrinopathy that is classically considered to be an isolated deficiency of cortisol production with normal electrolyte concentrations. Recent evidence suggests that insufficient aldosterone production is frequently present on AH diagnosis, regardless of measured electrolyte concentrations.[1] Because AH can present with various clinical signs or biochemical abnormalities, it is said to mimic many disease states, thereby obscuring consideration of AH as a differential. Confirmation is obtained generally by documenting a post-ACTH stimulated cortisol concentration of less than 2 µg/dL (55 nmol/L). However, suboptimal stimulation (>2 µg/dL [>55 nmol/L] but below the laboratory reference interval) provides equivocal diagnostic information.

This study retrospectively reviewed approximately 10 years' worth of medical records to extract clinical and biochemical data in dogs with confirmed AH (n = 40; stimulated cortisol concentration, 1-1.2 µg/dL [<28-33 nmol/L]) and suspected AH yielding suboptimal ACTH stimulation test results (n = 9; stimulated cortisol concentration, 3.4-8.1 µg/dL [94-223 nmol/L]).

Unlike previous reports in which female dogs were primarily affected, neutered male dogs comprised 57.5% of the AH group, with Labrador retrievers and standard poodles disproportionately affected. Clinical signs of both groups were nonspecific and chronic (present for >3 weeks), with lethargy and GI upset (eg, anorexia, vomiting, diarrhea) observed in most cases.

Hypoalbuminemia and hypocholesterolemia were the most common biochemical abnormalities detected in both groups and were encountered more frequently in confirmed AH dogs as compared with dogs suspected of having AH. Imaging was performed in only a minority of dogs in both groups, and small adrenal gland size was documented only in dogs with confirmed AH. Only 5 of 35 AH dogs developed a low sodium:potassium ratio (≤25.7) within 51 months of diagnosis. Daily physiologic glucocorticoid supplementation resolved clinical signs (30/31), hypoalbuminemia (25/27), and hypocholesterolemia (23/25) in AH dogs. At follow-up for 7 of the 9 dogs with suspected AH, none developed an electrolyte disorder. Several dogs with suspected AH (4/7) were eventually diagnosed with inflammatory bowel disease; clinical signs resolved for 2 of these dogs with no sustained therapy. One dog had persistent signs with no diagnosis obtained.

... TO YOUR PATIENTS

Key pearls to put into practice:

1. AH screening is warranted for patients presented with chronic lethargy or vague GI signs, hypoalbuminemia, and/or hypocholesterolemia.
2. Although electrolyte levels are commonly normal on AH diagnosis, assessment of pre- and post-ACTH stimulated aldosterone concentrations may more accurately reflect the patient's mineralocorticoid status.
3. Suboptimal ACTH stimulation test results may suggest the presence of another occult nonadrenal disease state (eg, enteropathy).

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Cat-to-Human H7N2 Infection

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In the Literature

Marinova-Petkova A, Laplante J, Jang Y, et al. Avian influenza A(H7N2) virus in humans exposed to sick cats, New York, USA, 2016. *Emerg Infect Dis*. 2017;23(12):2046-2049.

FROM THE PAGE ...

Influenza poses a tremendous public health burden, and extensive surveillance is used to detect emerging influenza threats.

Although influenza in cats is rare, a previous 2016 case report identified a large influenza outbreak in cats in a New York animal shelter.[1] The strain involved in this outbreak was an H7N2 avian influenza virus that had been identified in birds and a small number of humans in the early 2000s but had not been identified as part of large-scale testing (ie, 132 000-212 000 tests per day) in birds in the United States between 2007 and 2014.

The case report highlighted here discusses a veterinarian who had collected oropharyngeal samples from clinically normal cats at the shelter during the outbreak and subsequently developed influenza-like illness (eg, sore throat, muscle pain, cough).[1] When the virus was sequenced, human and feline isolates were found to be closely related to H7N2 strains that had been circulating in birds in the northeastern United States in the early 2000s. Although H7N2 is considered an avian influenza strain, feline and human isolates had changes in their genomes that enhanced the ability of the virus to attach to the mammalian respiratory tract and increase the risk for intramammal transmission. Although this strain had not been identified in the United States between the early 2000s and 2016, the genetic changes (ie, drift) present as compared with older strains suggest that it has continued to circulate, likely in wild birds.

... TO YOUR PATIENTS

Key pearls to put into practice:

1. Veterinarians may be at the forefront of exposure to new infectious disease risks.
2. Without testing of sick cats, this situation would have likely gone unidentified, as specific testing of the veterinarian occurred only because of the history of exposure to infected cats.
3. Veterinarians should be aware of zoonotic disease risks and ensure their healthcare providers are informed of any situations that might increase the likelihood of a zoonotic infection.

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1. Lee CT, Slavinski S, Schiff C, et al. Outbreak of influenza A(H7N2) among cats in an animal shelter with cat-to-human transmission-New York City, 2016. *Clin Infect Dis*. 2017;65(11):1927-1929.

Research Notes: Intralymphatic Immunotherapy in the Treatment of Canine Atopic Dermatitis

The study authors hypothesized that intralymphatic immunotherapy induces a better, more rapid response than do other types of immunotherapy for treating canine atopic dermatitis. Alum-precipitated allergen extract was injected into the popliteal lymph nodes of 51 participants. Twenty-two dogs completed the study and were included in a per-protocol analysis of results; all 51 participants were included in a separate intention-to-treat analysis. Pruritus and quality-of-life scores improved significantly in the intention-to-treat analysis; however, Canine Atopic Dermatitis Extent and Severity Index (CADESI) scores showed significant improvement only in the per-protocol analysis. Given the limited adverse effects, evaluation of intralymphatic immunotherapy as a safe, feasible, long-lasting treatment for canine atopic dermatitis is warranted.

Source

Timm K, Mueller RS, Nett-Mettler CS. Long-term effects of intralymphatic immunotherapy (ILIT) on canine atopic dermatitis. *Vet Dermatol*. 2018;29(2):123-e49.

High-Intensity Focused Ultrasound for Canine Solid Tumors

High-intensity focused ultrasound (HIFU) attacks cancer cells by using heat to cause thermal damage, coagulative necrosis, and cell death, leading to creation of a fibrous scar. In a clinical study, dogs received one to 3 treatments for solid tumors that were nonresectable and/or refractory to conventional chemotherapy. Tumor size decreased in 4 of 10 dogs; 2 of 10 dogs exhibited partial remission. All 4 dogs with bleeding from hemorrhagic tumors had alleviated clinical signs. Side effects (ie, hyperthermia, erythema, enteritis, skin ulceration) were mild and self-limiting. This study suggests that veterinary HIFU is a viable alternative treatment for dogs with solid tumors.

Source

Ryu MO, Lee SH, Ahn JO, Song WJ, Li Q, Youn HY. Treatment of solid tumors in dogs using veterinary high-intensity focused ultrasound: a retrospective clinical study. *Vet J*. 2018;234:126-129.

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Reference: 1. Mirataz™ (mirtazapine transdermal ointment) [package insert], Kindred Biosciences, Inc. (Burlingame, CA). Rev. 5/2018. **2.** Buhles W, Quimby JM, Labelle D, et al. Single and multiple dose pharmacokinetics of a novel transdermal ointment in cats. J Vet Pharmacol Ther. In press 2018.

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Canine Leptospirosis Update

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In the Literature

Knöpfler S, Mayer-Scholl A, Luge E, et al. Evaluation of clinical, laboratory, imaging findings and outcome in 99 dogs with leptospirosis. *J Small Anim Pract.* 2017;58(10):582-588.

Leptospirosis remains an important zoonotic disease. Clinical signs vary depending on geographic region and predominating serovar(s).

FROM THE PAGE ...

Leptospira spp of various serovars are responsible for human and animal leptospirosis infections worldwide. Leptospirosis remains an important zoonotic disease. Clinical signs vary depending on geographic region and predominating serovar(s). Disease should be suspected in patients with presence of common serum chemistry findings, including azotemia, increased liver enzymes, and/or hyperbilirubinemia. Leukocytosis, anemia, and thrombocytopenia are often found on CBC. Disease is confirmed with single microscopic agglutination titers ≥1:800 for nonvaccinal serovars, a 4-fold increase in microscopic agglutination titers over 2 to 3 weeks, or urine and blood PCR testing. Blood-based PCR can detect organisms in the first 10 days of infection, after which concentrations are highest in urine.[1] PCR tests are not influenced by vaccination,[2] but prior antibiotic administration can decrease sensitivity. Use of an immunoglobulin M-based screening test may also be useful for earlier detection.[3]

Although renal and hepatic involvement are most frequently reported, clinicians should be aware of potential for mild-to-severe pulmonary involvement. Multiorgan involvement of various combinations is common. Signs associated with lung involvement may be present at various times during disease progression. Thoracic radiographs should be obtained at initial presentation and if respiratory signs change during hospitalization. In this retrospective study, the medical records of 99 dogs with leptospirosis showed that 49% had pulmonary abnormalities detected on admission; nonsurviving patients more often had severe radiographic changes.

Treatment of leptospirosis includes amoxicillin-based drugs and doxycycline. Most patients require additional supportive care with IV fluids, gastroprotectants, and antiemetics. Those with pulmonary involvement may require oxygen therapy, and those with severe azotemia, those with significant metabolic abnormalities, or those progressing to oliguria or anuria may require hemodialysis. Patients requiring hemodialysis have a more favorable outcome than do patients receiving hemodialysis for other known or unknown causes.[4,5] Although many patients with leptospirosis can respond to treatment, the mortality rate can still be high, as represented by the 32% mortality rate in this study. Owners should be aware that multiorgan involvement, particularly in dogs with pulmonary manifestations, and more severe azotemia are factors associated with nonsurvival.

… TO YOUR PATIENTS

Key pearls to put into practice:

1. Because timing of *Leptospira* spp infection is often unknown, a combination of serologic and PCR testing at initial presentation may increase the likelihood of diagnosis.
2. Prognosis is more guarded for patients with more severe azotemia, multiorgan involvement, and pulmonary involvement.
3. If financially and geographically feasible, early referral for hemodialysis should be considered in patients not responding to conventional medical management.

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Nonopiate Alternative to Analgesia in Rabbits

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In the Literature

Schnellbacher RW, Divers SJ, Comolli JR, et al. Effects of intravenous administration of lidocaine and buprenorphine on gastrointestinal tract motility and signs of pain in New Zealand White rabbits after ovariohysterectomy. *Am J Vet Res.* 2017;78(12):1359-1371.

FROM THE PAGE ...

Opiates can have a number of adverse effects; ileus[1,2] and respiratory depression[3] are the most disconcerting of these effects in rabbits, making nonopiate-based analgesia desirable in this species.

This study provided a direct comparison of efficacy of buprenorphine versus lidocaine for both intraoperative and postoperative analgesia. All rabbits were administered ketamine and xylazine for induction and supplemental analgesia for ovariohysterectomy. Because pain can be difficult to assess in rabbits, a behavior-based system[4] to score comfort, similar to validated behavior-based systems in dogs,[5] was used in addition to traditional biochemical and physiologic pain assessment methods. Seven rabbits received buprenorphine (0.06 mg/kg IV q8h) for 2 days, and seven other rabbits received lidocaine as an intravenous bolus (2 mg/kg over 5 minutes) followed by a constant-rate infusion (100 µg/kg/min) for 2 days.

Intravenous lidocaine was found to provide significant improvement in pain control as compared with buprenorphine. Rabbits treated with lidocaine had decreased heart rates, lower serum glucose concentrations, and higher postoperative food intake and fecal production than did buprenorphine-treated rabbits, which suggests improved analgesia through lidocaine infusion. Levels of activity (play and exploring) and degree of observed comfort were also markedly improved in the lidocaine-treated group; recoveries were overall improved and patients appeared comfortable.

Results suggest that lidocaine provides an excellent alternative to buprenorphine analgesia in rabbit surgery. It may also provide means for controlling pain and inflammation, as well as the secondary consequences of both, in nonsurgical cases that require analgesia and control of ileus. Because postoperative ileus is common in rabbits, improved appetite and fecal production are good indicators of improved comfort. Based on this study and earlier publications, lidocaine administered as a constant-rate infusion would be a good first-line treatment protocol for GI stasis,[6] endotoxemia/dysbiosis,[7] and other causes of moderate-to-severe pain.

… TO YOUR PATIENTS

Key pearls to put into practice:

1. In rabbit medicine and surgery, adequate analgesia is a critical part of providing standard-of-care treatment; lidocaine can be a valuable tool in the application of nonopiate-based analgesia protocols.
2. Lidocaine provides a number of additional benefits for rabbits, including anti-inflammatory activity, free-radical scavenging, GI prokinetic function, and inhibition of endotoxin-related damage.[8-11]
3. Administration of lidocaine via a constant-rate infusion is a safe and effective analgesic method with fewer adverse effects than opiates in rabbits.
4. Intravenous lidocaine may be administered as part of a balanced therapy in nonsurgical cases of GI pain and ileus.

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Alternatives to Opioids for Perianesthetic Analgesia Management

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The current opioid shortage has resulted in challenges providing perioperative analgesia to dogs and cats. Although direct substitution is not appropriate for all situations, many alternatives are available.

To calm patients before and/or after anesthesia, gabapentin (5-10 mg/kg PO[1]) or trazodone (3-5 mg/kg PO[2]) may be used in cats and dogs, respectively. To the author's knowledge, serotonin syndrome has not been reported with trazodone use in veterinary medicine.

Oromucosal dexmedetomidine may also be considered for prearrival sedation (125 µg/kg oromucosal).[3] Oral acepromazine tends to have inconsistent effects, but injectable acepromazine (0.01-0.05 mg/kg IV, IM, or SC) is more reliable and may be used in patients that cannot receive oral medications.[4]

Other options, including alprazolam (0.01-0.02 mg/kg PO[5]), may be viable for some animals.

Oral Analgesia

Although popular, tramadol (5-10 mg/kg PO) has not been consistently reported to have good efficacy for pain management in dogs, as it has only weak opioid effects.[6] However, it may provide a sense of well-being based on its non-opioid (serotonergic- and norepinephrine-based) actions.[7,8] A serotonin-like syndrome has not been reported in animals but is theoretically possible when this drug is combined with similar medications (eg, trazodone, fluoxetine) or certain opioids (most notably meperidine).[7]

Perioperative NSAIDs (eg, carprofen [2.2-4.4 mg/kg PO or SC[9]], meloxicam [0.1-0.2 mg/kg PO or SC[10]], robenacoxib [1-2 mg/kg PO or SC[11]]) may also be considered in animals with no GI or renal disease and in the absence of steroid administration. The sooner in the course of anesthesia they can be administered so that tissue levels are reached, the more effective these medications are likely to be for postoperative pain management. It is important to remember, however, that hypotension under anesthesia may adversely affect renal blood flow and compound renal side effects.[12] Grapiprant (2 mg/kg PO[13]) is a newer noncyclooxygenase prostaglandin-receptor antagonist that has been shown to have efficacy in treating osteoarthritis pain in dogs. Its utility as a perioperative analgesic is not well studied, but an improved side effect profile may prove advantageous.[13]

Injectable Analgesia

Many µ-opioid agonists (eg, morphine, hydromorphone, oxymorphone, methadone, fentanyl, alfentanil, remifentanil, sufentanil) have been sporadically available. In addition to analgesia and variable degrees of sedation, they provide anesthetic-sparing effects while maintaining cardiovascular safety. For premedication and intraoperative use by infusion, these drugs are largely

interchangeable, provided the clinician has knowledge of their relative potency, onset and duration of action, and side effect profile.[6]

Buprenorphine (20-30 µg/kg IV, IM, or buccal), a partial µ agonist, may be used alone or in combination with other medications as a substitute for other µ agonists in dogs and cats for mildly-to-moderately painful procedures.[6,14] It may also be used with other drugs for more complex and painful surgical procedures to minimize pain. A dosing interval of approximately 6 to 8 hours has been suggested in the perioperative period.[14] Salivation, bradycardia, and respiratory depression may be observed with use; drug effects are generally not thought to be reversible. Sustained-release or long-acting formulations of buprenorphine for subcutaneous administration are available and are reported to provide between 24 and 72 hours of analgesia.[15,16]

Butorphanol (0.1-0.5 mg/kg IV, IM, or SC), a κ agonist and µ antagonist, is best used as a sedative and analgesic for presumed mildly painful procedures (eg, gastroduodenoscopy, colonoscopy, subcutaneous mass removal) or with adjunct analgesic techniques (eg, as a nerve block).[6]

Premedication with dexmedetomidine (3-10 µg/kg IM) can be considered in healthy dogs and cats to provide sedation and analgesia. Cardiovascular side effects may occur and present challenges with monitoring. If these effects are significant, partial reversal with atipamezole can lessen them; however alternative analgesia should be provided prior to reversal. Dexmedetomidine may also be administered as a constant-rate infusion in healthy dogs and cats; an initial maintenance dose of 1 µg/kg/hr IV has been suggested to provide analgesia and anesthesia-sparing effects.[17]

Infusion Analgesia

Ketamine is an *N*-methyl-D-aspartate–receptor antagonist that, at subanesthetic doses, has been shown to mitigate or prevent spinal facilitation of pain (ie, the *wind-up* effect). Although the drug is administered during anesthesia, the greatest benefit is thought to occur postoperatively.[18] However, even at low doses (eg, 10-20 µg/kg/min IV after a loading dose of 0.5 mg/kg IV), ketamine can reduce anesthetic requirements up to 25%.[19] Higher doses in dogs and cats have been reported to further reduce inhaled anesthesia requirements but exhibit a ceiling effect.[20] Although reports of benefits are largely anecdotal, ketamine infusions may be continued into the postoperative period in conscious animals. Doses of 1-3 µg/kg/min IV have been suggested to minimize behavior changes.[18] In patients for which preventing or reducing spinal facilitation is desirable but for which oral administration is preferred, amantadine (3 mg/kg PO q24h) may be considered.[21]

Intravenous lidocaine (2%) may be a cost-effective source of background analgesia and inhaled anesthetic dose reduction.[22] Side effects include seizures but are rare if clinically appropriate doses are used. Nausea may also be noticed at high doses in conscious patients. Anesthetic dose reduction with 50 µg/kg/min CRI IV (low end of the antiarrhythmic dose range) has been reported in dogs[19]; however, the authors' experience suggests that doses as low as 20-30 µg/kg/min IV are beneficial in clinical patients. Lidocaine is not routinely recommended for use in cats, as, despite a reduction in isoflurane dose, cardiovascular depression is greater with a combination of lidocaine and isoflurane than with an equivalent dose of isoflurane alone.[23]

Combinations of an opioid, lidocaine, and ketamine (opioid and ketamine for cats) may be used for their anesthesia-sparing effects to provide analgesia and reduce spinal facilitation of pain in dogs. When morphine, lidocaine, and ketamine are combined in dogs, the isoflurane dose is reduced by approximately 45%.[19] Respiratory depression is generally less than with high doses of opioids alone.

Higher doses of ketamine in dogs and cats have been reported to further reduce inhaled anesthesia requirements but exhibit a ceiling effect.[20]

Regional Anesthesia

Because of the shortage of drugs available for systemic administration, use of regional techniques (eg, injecting lidocaine [2%; up to 2 mg/kg] into the testicle prior to castration, providing a line block to the abdominal wall during an ovariectomy/ovariohysterectomy) when possible can be of significant benefit. Targeted nerve blocks and intra-articular or epidural administration provide other options for localized pain relief. Longer-acting local anesthetics (eg, ropivacaine, bupivacaine) may be used as warranted by the procedure and with consideration to duration of motor effects and toxicity.

Liposomal bupivacaine recently became available as another alternative for long-acting pain relief following surgery when injected into tissues at the surgical site.[24] Label directions should be followed if this drug is being used with other regionally or systemically administered local anesthetics.

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Suggested Reading

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Nutrition Assessment in a Dog with Sarcoma & Anemia

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

Gregg K. Takashima, DVM
WSAVA Global Nutrition Committee Series Editor

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Academy of Veterinary Nutrition Technicians

THE CASE

Kelsey, an 11-year-old spayed Maltese, was referred to a nutrition service for inappetence and weight loss one week post-splenectomy following a diagnosis of splenic histiocytic sarcoma. She was being treated postoperatively with lomustine (CCNU; 70 mg/m^2 PO q4wk). Before surgery, Kelsey weighed 12.1 lb (5.5 kg), but on presentation to the nutrition service, she weighed 11 lb (5 kg) and had a BCS of 3/9 (ideal BCS, 5/9) and a muscle condition score of moderate muscle loss (on a scale of normal, mild, moderate, to marked muscle wasting or

loss). Historic medical records showed the patient's weight typically ranged from 13.2 lb to 15.4 lb (6-7 kg), with an average BCS of 5/9; no muscle condition score had previously been documented.

Dietary History

Kelsey had reportedly been fed a variety of commercial dog foods until age 7. However, she reportedly did not appear to enjoy any of the commercial diets and was transitioned to a mixture of cooked tofu or cooked white fish with steamed vegetables offered ad libitum 3 times a day. The homemade diet did not contain any animal or human vitamin-mineral supplements. The owner reportedly did not offer treats or other human foods. Water intake was reported to be normal.

Preoperative serum chemistry profile and urinalysis results were normal, but CBC revealed microcytic hypochromic anemia and thrombocytosis. CBC with a reticulocyte count performed 2 weeks postsurgery (ie, 1 week after presentation to the nutrition service) showed further decrease in hematocrit and nonregenerative, microcytic hypochromic anemia (***Table 1***).

DIAGNOSIS:

SPLENIC HISTIOCYTIC SARCOMA & NONREGENERATIVE ANEMIA

Because Kelsey had been consuming an unbalanced homemade diet and had undergone surgical splenectomy, a serum iron panel was ordered and sent to a veterinary diagnostic laboratory to better characterize the nonregenerative, microcytic hypochromic anemia (***Table 2***).[1-4] Serum iron and total iron-binding capacity supported a diagnosis of iron deficiency anemia, although serum ferritin was slightly elevated. Serum ferritin is typically low in patients with iron deficiency anemia, as it correlates with body iron stores, but serum ferritin is an acute phase protein and may be elevated in patients with underlying disease such as neoplasia, liver disease, or hemolytic disease.[2-4] Hyperferritinemia has specifically been reported in dogs with histiocytic sarcoma and hemangiosarcoma.[5,6] Kelsey's discordant serum ferritin, although increased, was not as high as the values that have been reported with neoplastic disease and perhaps indicated concurrent disease effects.[4-6] It was postulated that Kelsey may have both anemia of chronic disease (secondary to

TABLE 1

CBC VALUE RESULTS OF IMPORTANCE

Test	Preoperative	2 Weeks Postsurgery	4 Weeks Postsurgery	2 Months Postsurgery	3 Months Postsurgery	Reference Range
Hematocrit	33%	27%	41.8%	41.6%	46%	41%-60%
Mean corpuscular volume	60 fL	59 fL	62 fL	73 fL	72.9 fL	62-74 fL
Mean corpuscular hemoglobin	22.3 pg	20.8 pg	23.6 pg	23.9 pg	24.6 pg	22-26.2 pg
Platelets	789 × 10^3/mL	939 × 10^3/mL	906 × 10^3/mL	707 × 10^3/mL	453 × 10^3/mL	147-423 × 10^3/mL
Reticulocytes	N/A	30.8 × 10^3/mL	149.6 × 10^3/mL	80.4 × 10^3/mL	106.3 × 10^3/mL	12.5-93 × 10^3/mL

neoplasia) and iron deficiency anemia (secondary to diet).[2,3,7]

Treatment & Follow-Up

Two iron dextran injections (20 mg/kg IM) were administered approximately one month apart at 2 weeks and 2 months postsplenectomy (***Table 1***), and a nutrition plan was instituted. The nutrition plan was formulated by a boarded veterinary nutritionist and included a complete and balanced homemade diet of cooked skinless chicken breast, sweet potato, vegetables, canola oil, and a vitamin-mineral supplement. The owner was given specific instructions for preparing the diet using cooked gram weights of each ingredient and was educated on the importance of adding the vitamin-mineral supplement. To ensure adequate intake of the homemade diet by the patient, the owner was given a computerized spreadsheet food journal to record daily gram intake. Three times a day, the owner offered the recommended gram amount of the recipe, weighed any food remaining, recorded the gram intake of each meal, then calculated total gram intake per day. The nutritionist reviewed the food journal weekly to ensure Kelsey was not only consuming the homemade diet but consuming adequate kcals for weight gain. Body weight was also reported to the nutritionist biweekly. Follow-up examination was conducted at 2 weeks and 1, 2, and 3 months after diet implementation to assess patient and owner compliance with the homemade diet. Food intake gradually increased, and at the 3-month recheck, the patient weighed 14.3 lb (6.5 kg) and BCS had improved to 4/9, although MCS remained at 2/3.

Follow-up CBCs showed a marked regenerative response and resolved anemia. The owner declined a repeat serum iron panel due to financial constraints but reported that the dog's appetite had improved after the iron injections and implementation of the nutrition plan.

Repeat diagnostics and imaging after 9 months of lomustine therapy showed no evidence of histiocytic sarcoma; thus, the oncology service recommended discontinuing treatment. The owner was counseled to continue the homemade diet as outlined and to contact the nutrition service if there were any changes in the patient's medical condition. Two and half years after cancer diagnosis, Kelsey was euthanized for poor quality of life with no specific diagnosis.

Conclusion

This case illustrates the importance of nutritional assessment and management in veterinary cancer patients. Veterinary patients can often sustain a reasonable quality of life on an unbalanced diet, but in patients with neoplasia, inadequate nutrient intake can impact patient outcomes and quality of life. Anemia is common and is most often assumed to be anemia of chronic disease. An in-depth dietary history and further laboratory assessment of nutritional status can help identify dietary factors that can affect quality of life in cancer patients. This case also illustrates the importance of providing nutritional follow-up when prescribing a homemade diet, as nutritional follow-up can help ensure owner compliance and that the nutritional goals—in this case, weight gain and resolution of anemia—are met.

TABLE 2

SERUM IRON PANEL RESULTS

Test	Result	Reference Range
Serum iron	30 µg/dL	33-147 µg/dL
Total iron-binding capacity	298 µg/dL	282-386 µg/dL
Serum ferritin	811 ng/mL	80-800 ng/mL

Continues ▶

ASK YOURSELF ...

QUESTION 1

Anemia of chronic disease is typically represented by:

A. Normocytic, normochromic anemia
B. Nonregenerative anemia
C. Low serum iron and high ferritin
D. All of the above

MOST ACCURATE ANSWER: D

Anemia of chronic disease is the most common cause of nonregenerative anemia. It is characterized by mild-to-moderate normocytic, normochromic anemia with low serum iron and high ferritin levels.[4]

QUESTION 2

Iron deficiency anemia is best described as:

A. Regenerative or nonregenerative microcytic hypochromic anemia, thrombocytosis, and low serum iron
B. Nonregenerative microcytic hypochromic anemia with low serum iron and high serum ferritin
C. Regenerative microcytic hypochromic anemia with concurrent pancytopenia
D. Nonregenerative macrocytic anemia and thrombocytopenia with low cobalamin

MOST ACCURATE ANSWER: A

Iron deficiency anemia can be regenerative then progress to nonregenerative. It is characterized by microcytic hypochromic RBCs, low hemoglobin, low serum iron, and low serum ferritin. Thrombocytosis can also be observed with many large platelets.[4]

QUESTION 3

Thrombocytosis can be observed with:

A. Endocrine disease
B. Iron deficiency anemia
C. Immunosuppressive therapy
D. All of the above

MOST ACCURATE ANSWER: D

Thrombocytosis is common and can be observed with iron deficiency anemia, endocrine disease, splenectomy, neoplasia, and immunosuppressive therapy (eg, prednisolone, vincristine).[8]

QUESTION 4

Which of the following statements regarding the risks associated with parenteral iron in veterinary medicine is correct?

A. Iron overload is a common problem in both dogs and cats.
B. Anaphylaxis is common.
C. Pain or soreness at the injection site may occur.
D. Acute vomiting and diarrhea are frequent side effects.

MOST ACCURATE ANSWER: C

Dogs and cats are relatively resistant to iron overload. Anaphylaxis is a rare complication with parenteral iron. Gastric upsets may be observed with oral iron administration, whereas pain or soreness may be observed with intramuscular injections.[3]

QUESTION 5

Which of the following in a dietary history should increase concern for potential nutritional problems?

A. A homemade diet
B. A raw diet
C. Frequent and large quantities of treats, snacks, or table food
D. All of the above

MOST ACCURATE ANSWER: D

Patients on any of these diets are at risk for important nutritional deficiencies and excesses, and a thorough nutritional assessment is indicated.

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TOP 5

TOP 5 ZOONOTIC DISEASE CONCERNS IN HOSPITAL VISITATION DOGS

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A variety of animals may be encountered in human healthcare facilities, including service animals, patients' pets, therapy animals for animal-assisted therapeutic activities, and visitation animals.[1] The latter category, typically pets of volunteers brought to facilities to interact with patients, is the most common and the focus of this discussion.

Animal visitation programs, also referred to as *pet therapy* or *animal-assisted activities*, can have various positive impacts on patients[2-5]; however, any human–animal contact poses some degree of risk for transmission of zoonotic pathogens. Healthcare facilities contain large numbers of individuals with increased susceptibility to disease, heightening zoonotic disease concerns.

Most animals used for animal visitation programs are dogs, a relatively low-risk species for which there is a good understanding of pathogen carriage rates and risk factors and an ability to test temperament. Therefore, this article focuses on zoonotic concerns pertaining specifically to dogs.

A variety of bacteria, viruses, and fungi pose some degree of zoonotic risk, but the primary concerns typically involve opportunistic bacterial pathogens.

TOP 5 ZOONOTIC DISEASE CONCERNS IN HOSPITAL VISITATION DOGS

1. Methicillin-Resistant *Staphylococcus aureus*
2. *Clostridium difficile*
3. Extended-Spectrum β-Lactamase–Producing Enterobacteriaceae
4. *Salmonella* spp
5. Exposure to Pathogens from Bites & Scratches

PATHOGEN SCREENING

In general, pathogen screening is not considered useful because it shows a result from a single point in time and uses tests that are not 100% sensitive and cannot test for the wide array of potentially zoonotic pathogens. A negative result would show that the dog was "probably" negative (for the tested pathogens only) at the time of sampling but could have been exposed any time thereafter. A negative result would *not* show that the dog is not carrying a pathogen, that it poses no risk, or that precautions such as hand hygiene are not needed because of the range of other pathogens. Because pathogen screening does not modify required practices and can be expensive, the benefit is limited.

The incidence of dog-associated disease in healthcare facilities is unknown, possibly because it is rare. However, it is likely that infections occur, at least sporadically, and are undiagnosed. This is particularly true for pathogens that are common in hospitalized individuals (eg, multidrug-resistant bacteria), as identification of an infection might not trigger much investigation or consideration of potential animal sources. A collection of basic infection control and visitation practices can presumably reduce the risks that may be encountered.[1]

Following are the author's top 5 zoonotic disease concerns in hospital visitation dogs. Because evidence is empirical, this list is based on conjecture rather than data.

1 Methicillin-Resistant *Staphylococcus aureus*

Methicillin-resistant *Staphylococcus aureus* (MRSA) is a leading cause of hospital-associated infection in humans. This multidrug pathogen can colonize the nose, throat, skin, and GI tract of dogs and humans in the absence of disease. MRSA colonization has been identified in a small percentage of dogs and typically involves the same strains that infect humans.[6-9] These cases presumably occurred predominantly from human–dog transmission, but colonized dogs could be sources for subsequent infection of humans.

Hospital visitation dogs have been shown to be at elevated risk for MRSA colonization, presumably from contact with colonized patients.[10] Transient contamination of the haircoat can also occur during patient contact.[11]

Screening of visitation dogs for MRSA carriage is not recommended (see ***Pathogen Screening***).[1] MRSA prevention should be focused on practicing good hand hygiene before and after animal contact. Because antibiotic exposure increases the risk for MRSA colonization in dogs,[10] short-term exclusion of dogs that are receiving or have recently received antibiotics is recommended.[1] Dogs that participate in hospital visitation pro-

grams are more likely to encounter MRSA than are nonparticipating dogs; thus, culture and susceptibility testing of wound infections and other bacterial infections is warranted. Dogs with any wound infections should be excluded from visitation because of the potential involvement of pathogens such as MRSA, as well as the risk for exposure to other pathogens that could complicate the wound infection.

2 *Clostridium difficile*

Clostridium difficile is an important cause of morbidity and mortality in hospitalized humans. This fecal–oral pathogen can also be found in the GI tract of healthy dogs and humans.[12-15] Zoonotic transmission from dogs has not been clearly established, but the same strains have been found in dogs and humans.[16-18]

Hospital visitation dogs are at significantly elevated risk for *C difficile* shedding,[10] likely acquired through ingestion of *C difficile* spores from the hospital environment and patient hands. Risk reduction involves limiting exposure of dogs (eg, not visiting patients who are under enhanced precautions for *C difficile* infection, encouraging patients to practice good hand hygiene before contact with a dog, limiting contact with patients' living spaces) and reducing dog–human transmission (eg, through good fecal handling, preventing fecal accidents, and practicing good hand hygiene). As with MRSA, short-term exclusion of dogs that are receiving or have recently received antibiotics is recommended.[1] Screening of animals for *C difficile* shedding is not recommended (see ***Pathogen Screening***).

3 Extended-Spectrum β-Lactamase–Producing Enterobacteriaceae

A variety of multidrug-resistant gram-negative bacteria are important causes of infection in healthcare facilities, with some strains being near pan-resistant (ie, resistant to all available antimicrobials). Extended-spectrum β-lactamase (ESBL)–producing bacteria are widely distributed in healthy dogs, and strains that cause disease in humans are often identified in dogs,[19,20] which suggests the potential for both human–dog and dog–human transmission in healthcare facilities. Other resistant gram-negative bacteria that may be encountered include carbapenemase-producing Enterobacteriaceae, which may be extensively drug resistant. Colonization or infection of dogs with carbapenemase-producing Enterobacteriaceae is rare but possible,[21,22] and because these pathogens are increasingly found in human healthcare facilities, the potential for exposure and colonization in the GI tract is increased.

Because ESBL-producing bacteria are fecal–oral pathogens, preventive measures are similar to those described for *C difficile*, and screening of visitation animals is not recommended (see ***Pathogen Screening***). Exclusion of dogs actively or recently (ie, within the past month) treated with antimicrobials is recommended,[1] as antimicrobial exposure is a risk factor for ESBL acquisition[23,24] and, presumably, acquisition of other resistant gram-negative enteric pathogens.

4 *Salmonella* spp

Salmonellosis can be life-threatening in compromised dogs and humans. Although the prevalence of *Salmonella* spp shedding tends to be low in healthy adult dogs, higher rates can be found in some subpopulations, particularly dogs fed raw meat-based diets or treats.[25-27] Risk reduction involves prohibition of raw meat and/or raw animal-based treats to visitation dogs and exclusion of dogs with active or recent (ie, within the past week) diarrhea.[1] Good fecal handling practices and attention to hand hygiene can help further reduce the risk. Routine testing for *Salmonella* spp is not recommended (see ***Pathogen Screening***); however, culture or PCR testing of diarrheic therapy dogs may be useful in identifying animals that require a longer exclusion period after resolution of diarrhea.

ESBL = extended-spectrum β-lactamase
MRSA = methicillin-resistant *Staphylococcus aureus*

5 Exposure to Pathogens from Bites & Scratches

Although often overlooked in discussion of zoonotic diseases, bites and scratches may be the most common and potentially serious hazards associated with visitation dogs. The incidence of bites and scratches in healthcare facilities has not been reported, but they have been observed.[28] Bites are of particularly high risk because of the myriad opportunistic pathogens found in a dog's mouth, such as *Pasteurella* spp and *Capnocytophaga canimorsus*. Bites can also inoculate pathogens (eg, MRSA) that might be residing on a human's skin.[29] Scratches from dogs pose a lower risk for infection as compared with bites but can cause pain, and any disruption of the protective skin barrier may increase the risk for infection in high-risk individuals.

MRSA = methicillin-resistant *Staphylococcus aureus*

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Today's veterinarian should consider inappetence as a spectrum that can vary depending on the degree of appetite reduction. Inappetence is commonly associated with anorexia or a lack of appetite leading to no food intake, but it is equally important to recognize and address hyporexia (ie, a decreased appetite leading to decreased food intake) and dysrexia (ie, a change in appetite that results in an altered food intake).[1]

There are many potential causes of an altered or absent appetite in dogs. Chronic or systemic conditions may include chronic kidney disease (CKD), cancer, infectious disease, or aging. Acute conditions may include pain, nausea, dehydration, fever, and postoperative ileus.[2] Early recognition of inappetence and implementing appropriate nutrition is essential as a long-term poor nutritional state may result in weakness, muscle loss, decreased ability to heal, and overall increased patient morbidity.[3]

A pet that is unwilling to eat or no longer seems excited to eat is a major concern for clients; clients may also perceive an inappetent pet to have a diminished quality of life, particularly if concurrent weight loss and lethargy are present.[3] Necessary medications may be challenging to administer if the patient does not readily accept them in food, and all benefits of a prescription diet are lost if the patient is not eating or consuming enough to meet its daily energy needs, or minimum energy requirement (MER).[4]

Practitioners should be diligent in educating the team and clients to recognize inappetence and understand the nutritional requirements of each patient. Key indicators of inappetence are frequently overlooked in a patient's history because they are considered by the owner as variations of normal. In order to avoid missing vital information, every appointment should obtain the following information to ensure a full nutritional assessment.

Food Type Consumed Daily

- *Considerations:* Is the diet complete and balanced to provide adequate nutritional intake for this patient?
- *Action:* Instruct all clients to bring photos or samples of pet food labels to every appointment. Train team members to identify and confirm AAFCO nutritional adequacy statements.[5]

Amount of Food Consumed Daily

- *Considerations:* Is this amount of the diet complete and balanced to provide adequate nutritional intake? Are the patient's MER and resting energy requirement (RER) being met?
- *Action:* Train team members to quickly and easily calculate a patient's RER (kcals).[4]

Calculating Minimum and Resting Energy Requirements[4]
RER = (BW in kg × 30) + 70
MER (kcal) = Appropriate multiplier to RER

Owner Assessment of Appetite

- *Considerations:* Does the patient seem to be a selective eater? Does the owner find it necessary to routinely change diets to keep the pet interested in eating? Is the patient excited for treats but not for a balanced diet?
- *Action:* Make strong recommendations for complete and balanced diets[4] that are highly palatable. Advise owners to make any food changes gradually (over several days) in order to avoid potential GI upset, which can lead to subsequent food aversion.

Weight History

- *Considerations:* Is the patient losing weight without any intentional efforts by the owner?
- *Action:* Provide clients with a printed weight history and body condition score (BCS) chart at each appointment. Pursue full diagnostic work-ups to determine underlying causes as needed.

Body and Muscle Condition Scores (BCS, MCS)

- *Considerations:* Body condition and muscle condition scores can change with or without concurrent weight loss.[7] These assessments can help indicate how inappetence should be addressed.
- *Action:* Ensure clients understand that BCS is a subjective assessment of body fat and MCS is a subjective assessment of body muscle.[6]

Conclusion

Implementing clear protocols with the practice team and educating clients will ensure that early recognition of inappetence begins at home and can be confirmed in the examination room. Treatment of the underlying causes and use of an appetite stimulant when indicated will ensure that dogs live healthier, happier days than when clinically unwell. Entyce is the only appetite stimulant developed, field-tested, labeled, and FDA-approved for use in dogs with inappetence.[3]

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See page 62 for product information summary.

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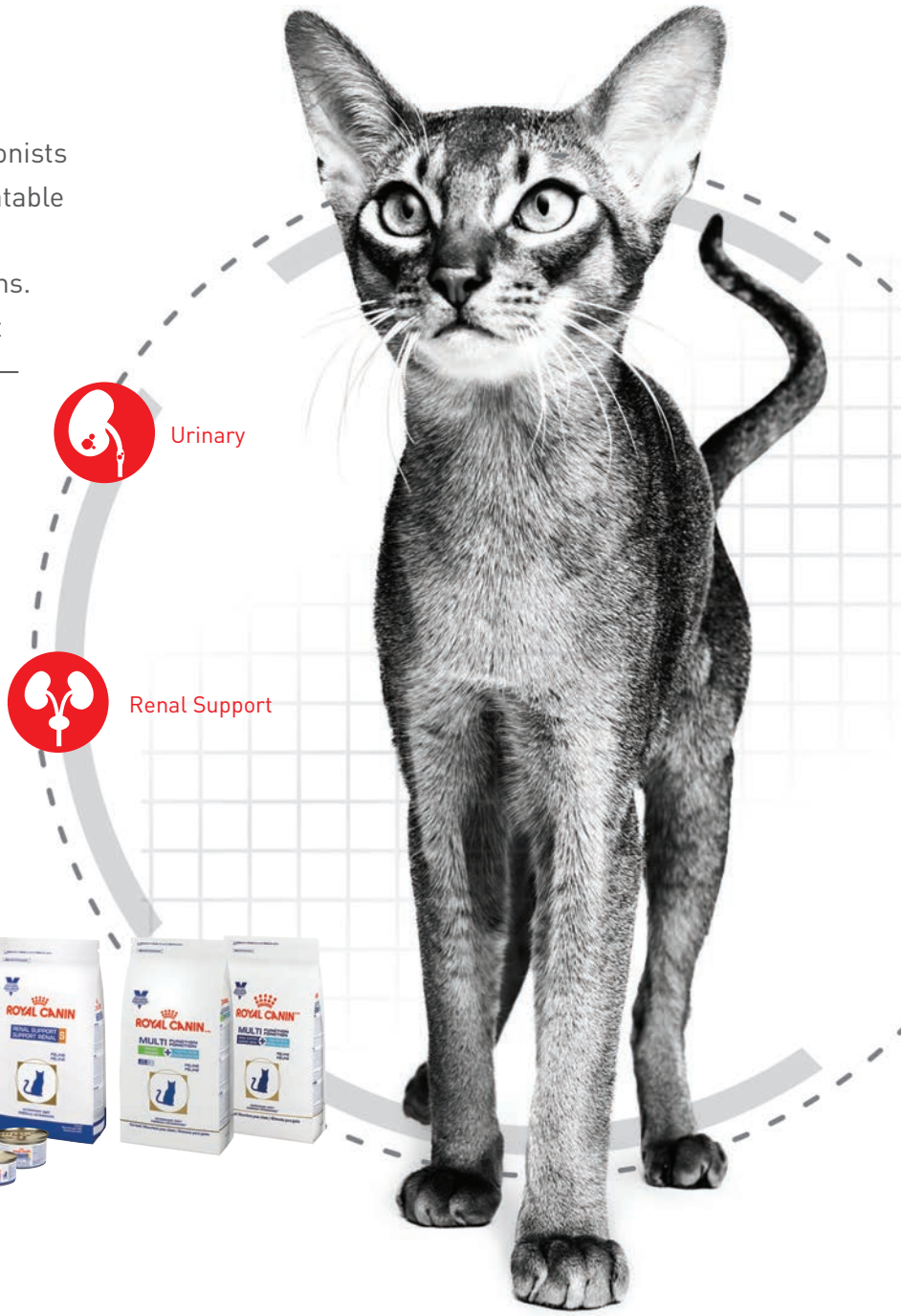

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Featured Formulas:

Hypocobalaminemia

Leonard E. Jordan, DVM
M. Katherine Tolbert, DVM, PhD, DACVIM (SAIM)
University of Tennessee

Background & Pathophysiology

Cobalamin (ie, vitamin B_{12}) is a water-soluble vitamin that plays an important role in DNA and RNA synthesis, amino acid (eg, cysteine, homocysteine) metabolism, and energy production. Following ingestion of cobalamin-rich nutrients (eg, fish, poultry, eggs, red meat, dairy products), cobalamin first binds to haptocorrin, which is produced in both the salivary gland and the stomach. In the duodenum, cobalamin is bound to intrinsic factor—a protein produced primarily in the pancreas of dogs and cats—and is later absorbed in the distal small intestine.

Any disease that affects the production of intrinsic factor or interferes with the intestinal absorption of cobalamin can cause cobalamin deficiency (***Table***, next page). Dogs and cats with exocrine pancreatic insufficiency (EPI) may have decreased production of intrinsic factor. Intestinal diseases (eg, inflammatory bowel disease, food-responsive enteropathy, intestinal lymphoma, dysbiosis, lymphangiectasia) can result in compromised ileal function and inadequate absorption of cobalamin.[1,2] Familial cobalamin deficiency resulting from a loss-of-function mutation in the receptor responsible for intestinal cobalamin absorption is an uncommon cause of hypocobalaminemia but should be considered in young patients presented with GI and neurologic signs, especially in predisposed breeds such as giant schnauzers, Australian shepherd dogs, border collies, beagles, shar-peis, and Komondors.[3,4]

EPI = exocrine pancreatic insufficiency

History & Clinical Signs

Common signs of cobalamin deficiency in dogs and cats include GI signs (eg, anorexia, weight loss), which often mimic those observed in animals with chronic GI disease; thus, the clinician may not immediately consider cobalamin deficiency as a contributing factor. Additional clinical signs of hypocobalaminemia can include failure to thrive, immunodeficiency, and neuropathies. These clinical signs may be more commonly observed in dogs with familial cobalamin deficiency. Unlike those occurring with pancreatic and GI disease, clinical signs induced by familial hypocobalaminemia are responsive to cobalamin supplementation alone.[5] In one case report, a border collie with selective cobalamin malabsorption was presented with hepatic encephalopathy secondary to hypocobalaminemia, which resolved following cobalamin supplementation.[6] In another report, a Yorkshire terrier with selective cobalamin malabsorption was presented with seizures that also resolved with parenteral cobalamin supplementation.[7] Thus, cobalamin deficiency should be considered in any animal presented with chronic GI signs, especially when in combination with neurologic signs.

TABLE

DISEASES ASSOCIATED WITH LOW COBALAMIN

Disease	Diagnostic Test(s)
Exocrine pancreatic insufficiency	Trypsinogen-like immunoreactivity
Pancreatitis	Pancreatic lipase immunoreactivity, abdominal ultrasonography
Inflammatory bowel disease	Intestinal biopsy and histopathologic examination
Intestinal lymphoma	Intestinal biopsy and histopathologic examination ± immunophenotyping, PCR for antigen receptor rearrangements (PARR)
Lymphangiectasia	Abdominal imaging, intestinal biopsy and histopathologic examination
Selective cobalamin malabsorption	Genetic testing for some patients (eg, evaluation for cubilin [*CUBN*] gene mutation), urine MMA testing

Diagnosis

Hypocobalaminemic cats often do not respond as readily as normocobalaminemic cats to treatment of the primary disease unless supplemented with cobalamin; this is unproven but, in the authors' clinical experience, is also suspected in hypocobalaminemic dogs. Thus, cobalamin deficiency is an important clinical consideration in any patient presented with signs of chronic enteropathy or pancreatic disease. Diagnosis of hypocobalaminemia requires measurement of serum cobalamin concentrations. However, patients may have serum cobalamin levels that are low-normal (250-350 ng/L) and still have critically low tissue cobalamin concentrations. In these cases, evaluating biomarkers of tissue cobalamin deficiency (eg, methylmalonic acid [MMA], homocysteine) may provide more insight, as these biomarkers often increase with tissue cobalamin deficiency in dogs.[4,8-10] In cats, MMA may be a better indicator of tissue cobalamin deficiency as compared with homocysteine.[6]

Treatment & Management

Cobalamin therapy (see ***Suggested Reading***, page 51, for dose, frequency, and administration information) should be instituted when serum concentrations fall below 250 ng/L. Additional consideration for supplementation is recommended in patients with a low-normal serum cobalamin (250-350 ng/L) and/or signs of intestinal or pancreatic disease. Hypocobalaminemia secondary to GI disease has anecdotally been thought to require parenteral supplementation of cobalamin until the intestinal or pancreatic disease was appropriately treated because of the inability to absorb cobalamin or produce intrinsic factor, respectively. However, recent research has suggested that oral administration of cobalamin in dogs and cats with chronic enteropathies[11,12] and dogs with EPI[13] is effective in restoring normal cobalamin concentrations. This may be secondary to enhanced passive absorption of cobalamin along the length of the small intestine.

Prognosis & Prevention

The prognosis for hypocobalaminemic patients depends largely on the underlying disease process and how the patient responds to treatment of the primary disease. Low cobalamin concentration is associated with shorter survival with some diseases, including EPI and multicentric lymphoma.[13,14] Lack of recovery for dogs with chronic diarrhea due to inflammatory idiopathic or neoplastic disease may also be more likely when severe hypocobalaminemia (<200 ng/L) is present.[15] The benefit of supplementation in these disease states has not been definitively proven; however, it is recommended to evaluate the patient's serum cobalamin concentration and provide supplementation when hypocobalaminemia is identified. Prognosis for familial cobalamin deficiency is good with long-term supplementation.

Clinical Follow-Up & Monitoring

Daily oral cobalamin supplementation or a 6-week course of weekly parenteral supplementation followed by a single injection 30 days later and retesting after 30 days is recommended.[1,16] Some patients, especially those with EPI or ongoing intestinal disease, may require continued monthly cobalamin supplementation. If resolution of the primary disease cannot be achieved, more frequent cobalamin administration may be required. If remission of the underlying disease (eg, food-responsive enteropathy) is achieved, long-term supplementation may not be necessary; however, re-evaluation of the patient's serum cobalamin concentration is recommended if disease relapse occurs.

EPI = exocrine pancreatic insufficiency
MMA = methylmalonic acid

See page 51 for references.

Pulmonary Barotrauma & Pneumothorax During Anesthesia

Marlis Rezende, DVM, PhD, DACVAA
Colorado State University

In anesthesia, the term *barotrauma* is used to describe lung tissue trauma resulting from excessively high airway pressure associated with excessive inflation of the lungs and alveolar overdistension, which can result in alveolar and pleural rupture.[1,2] When alveolar rupture occurs, air leaks into the pleural space and creates a closed pneumothorax, which in turn can rapidly evolve into a tension pneumothorax, especially if mechanical ventilation is being used. The resulting excessively high intrathoracic pressure impairs venous return to the heart, severely compromising stroke volume and cardiac output. If not quickly recognized and corrected, life-threatening cardiovascular collapse can occur.[2]

Causes of Barotrauma

Although an inadvertently closed pop-off valve is regarded as the most common cause for pulmonary barotrauma and pneumothorax during anesthesia, clinicians should be aware of other potentially dangerous scenarios that could lead to alveolar overdistension and rupture. Equipment-related barotrauma is typically caused by either excessive gas inflow into the breathing circuit and airway or restriction/obstruction of the gas outflow pathway.[3,4]

Excessive Inflow of Gas

Excessive inflow can occur from improper use of the oxygen flush valve, aggressive ventilator settings (high airway pressures and tidal volumes), and/or inappropriate connection of oxygen tubing (meant for oxygen insufflation via open mask) to a cuffed endotracheal tube, laryngeal mask airway, or other airway device without the ability to allow excess gas to vent.

The oxygen flush valve allows oxygen at high pressure and volume into the breathing system (35-70 L/min with a pressure of 45-60 pounds per square inch gauge [PSIG], which becomes approximately 1 L/s into the breathing system).[3,4] A nonrebreathing system (eg, Bain breathing system) has a relatively small inner volume and little compliance. Therefore, use of the flush valve while a patient is connected to a nonrebreathing system transmits excess volume and pressure directly to the patient's airway and lungs. Similarly, if the oxygen flush valve is used during the inspiratory phase of mechanical ventilation, the patient's lungs may be exposed to excessive pressure and overdistension. During the inspiratory phase, the ventilator's driving pressure actively compresses the bellows to deliver a breath, and the ventilator's exhaust valve is closed. Because the ventilator's driving pressure (65-75 cm H_2O) prevents the expansion of the bellows until breathing system pressures overcome the driving pressure, activation of the flush valve at this time (eg, to reinflate the bellows after a brief disconnection) would direct all the volume and resulting pressure to the breathing circuit.[3]

Aggressive Ventilator Settings

Inappropriately performed or overly aggressive mechanical ventilation can also cause barotrauma. In contrast to spontaneous ventilation, in which inspiration relies on the negative intrathoracic pressure generated by chest expansion to passively inflate the lungs, mechanical ventilation actively inflates the lungs using positive pressure. If excessive high tidal volumes and/or peak inspiratory (and plateau) pressures are used, barotrauma may occur. Overzealous manual breaths can have similar effects, when high tidal volumes and/or airway pressures are generated.

Outflow Restriction or Obstruction

Any form of significant breathing circuit outflow restriction or occlusion can lead to excessive airway pressures and lung overinflation, as there is no path to release the excess gas from the breathing system. Common examples include pop-off valve obstruction, compression or kinking of the scavenger hose, obstruction of the F/AIR anesthesia gas filter canister vents, and kinking of the hose that connects the ventilator to the breathing circuit. Additional care should be taken when using nonrebreathing systems, as the combination of the required high fresh gas flow rates with the relatively small inner volume of the breathing circuit allows airway pressures to rise very quickly in the case of an obstruction.

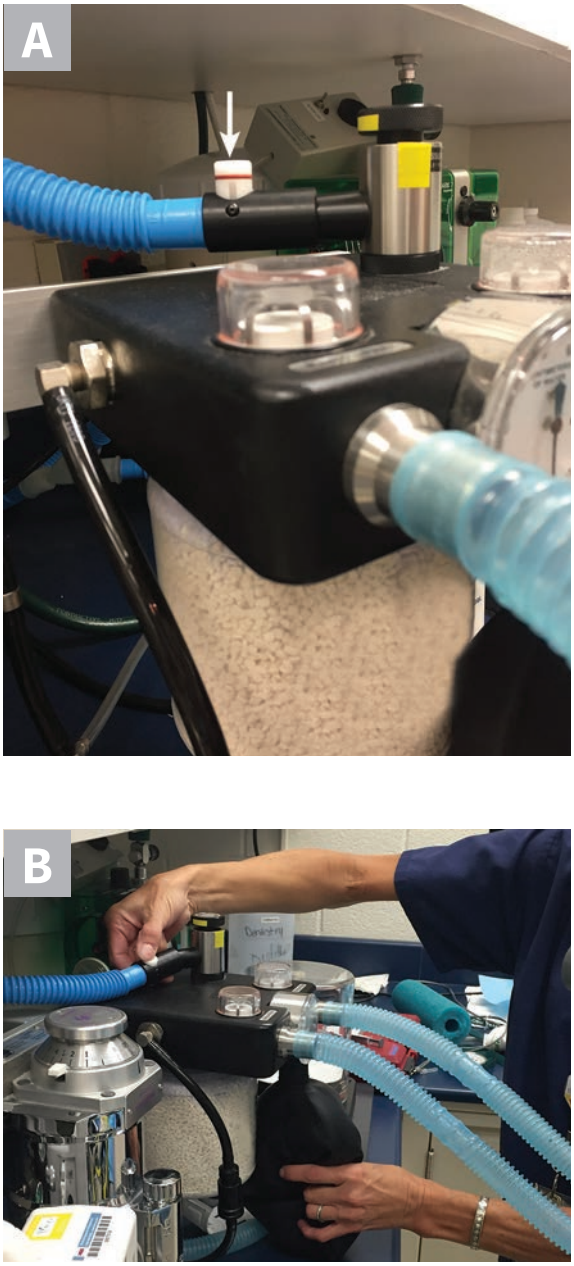
Patients at Increased Risk

Pre-existing lung disease (eg, pulmonary bullae, pneumonia, acute respiratory distress syndrome, feline asthma) may predispose animals to barotrauma and pneumothorax under anesthesia.[2] Other pre-existing conditions,

SAFETY DEVICES TO PREVENT BAROTRAUMA

Most anesthesia-associated barotrauma events (and resulting pneumothorax) can be avoided through both a functional understanding of the anesthesia machine and the presence of safety features designed to prevent harmful conditions or alert the team if such conditions arise, including:

- Pop-off occlusion valve (***Figure 1***, next page). This device can be attached to the outflow port of the anesthesia machine's original pop-off valve. When the top button of the valve is pushed, flow out of the pop-off valve is occluded and a manual breath can be administered. Once the button is released, flow through the valve is automatically re-established, minimizing the risk for forgetting to reopen the original pop-off valve, as it will always be left open. Although this can be useful during spontaneous ventilation, it does not completely eliminate the risk, as the original pop-off valve will still need to be closed (and opened afterward) if mechanical ventilation is to be used or during the process of pressure checking the anesthesia machine for leaks.
- High-pressure alarm (***Figure 2***, page 71). This device provides an audible alarm when the breathing circuit pressure reaches a set level (typically 20 cm H_2O). In addition, it can be used with both rebreathing and nonrebreathing systems with spontaneous or mechanical ventilation. The device will alarm when a dangerous breathing circuit pressure occurs (independent of cause), providing the clinician time to intervene.



▲ **FIGURE 1** Pop-off occlusion valve open (***A***; ***arrow***) and actively closed while giving a manual breath (***B***)

although not a consequence of true barotrauma, may increase the risk for a pneumothorax due to pulmonary tissue fragility or injury. This is especially notable in patients that have undergone trauma to the chest (eg, hit by a car, kicked by a horse), as the pulmonary contusions create areas of alveolar fragility.[5] Patients with pulmonary neoplastic masses, cysts, abscesses, or foreign body migration can be similarly predisposed to pneumothorax despite appropriate ventilation settings.

Pneumothorax

Pneumothorax is a life-threatening complication of barotrauma. Awareness and early recognition are key to a successful outcome. During anesthesia, a closed pneumothorax can rapidly evolve to a tension pneumothorax. In a *one-way valve* mechanism, air leaks out during lung inflation. As the lung tissue recoils during exhalation, air cannot escape via its entry path and becomes trapped outside the lungs in the thoracic cavity. The high-pressure intrathoracic environment that soon develops limits lung expansion and, most importantly, prevents venous return to the heart, leading to cardiovascular collapse.

As the lungs' ability to expand decreases and atelectasis increases, a change in breathing pattern typically occurs, followed by dyspnea and a decrease in oxygen saturation. As the pneumothorax evolves to a tension pneumothorax and venous return is compromised, severe hypotension and hypoxemia occurs. Reflex tachycardia may be present. The patient becomes more difficult to ventilate as lung compliance decreases and chest wall movement is diminished. On auscultation, lung sounds may be absent or significantly diminished.

Early recognition of clinical signs can be hindered in cases in which the patient's overall condition is already compromised (eg, patient in shock, with hypovolemia, and/or with significant intraoperative blood loss). Pneumotho-

rax may only become evident on cardiopulmonary collapse. It is therefore important that the clinician is aware of the potential risk for a pneumothorax based on the patient history and potential predisposing conditions.

If a pneumothorax is suspected, positive pressure ventilation should be immediately discontinued and thoracocentesis performed for emergency decompression of the chest. Once the intrathoracic pressure is relieved, arterial blood pressure and oxygen saturation will improve. A thoracostomy tube should then be placed to allow air to be continuously removed until the ruptured alveoli can seal to prevent the reoccurrence of a tension pneumothorax. (For a detailed description of how to perform a thoracocentesis or place a thoracostomy tube, see ***Suggested Reading***.)

Conclusion

Understanding and ensuring the proper functioning of the anesthesia machine before each use, adding safety features to help prevent and/or recognize mistakes, and having a dedicated individual to monitor anesthesia who is able to rapidly recognize equipment issues and adverse events are key to increasing patient safety.

▲ **FIGURE 2** High-pressure alarm and tubing (***arrow***) that is connected to the anesthesia machine's fresh gas outflow

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Interview with Paul Sessa, DVM

Evolution of Surgical Laser Technology

By Anya Glazkova, PhD

Our interview with Paul Sessa, DVM, highlights his transition from the older generation surgical CO_2 laser to a newer higher power surgical laser platform based on flexible fiber beam delivery with tipless handpieces.

Q: Dr. Sessa, you have had a flexible-waveguide CO_2 laser for over 10 years. Why did you choose the flexible waveguide laser over the articulated arm one? Also, what differentiates the CO_2 laser surgery from diode or even electrocautery systems?

A: Simply put, the articulated arm systems represent outdated technology. I mean, how do you even compare holding a state-of-the-art, pen-like handpiece to operating a bulky, heavy articulated arm? And that aiming beam does not even come close to the flexibility, the finesse that you are able to achieve with the flexible waveguide. As far as diode lasers and electrocautery are concerned, they simply cause more thermal damage to adjacent tissue. Compared to electrocautery in particular and some diode lasers, my CO_2 laser does not mechanically traumatize tissue - it is a non-contact approach.

Q: Dr. Sessa, how often do you use your laser?

A: We use it for about 10 surgeries per week. The benefits of the laser for pets are important to our clients. Laser surgery certainly differentiates us from other veterinary practices in our area, and that's a big deal. I think I've forgotten how to use a scalpel blade… and I'm not missing it!

Q: How do the two laser systems compare?

A: The new Aesculight is a huge leap forward - the greater cutting power, more flexibility, considerably less char, the benefits of the new adjustable handle, the built-in clinical library… My older Luxar LX-20SP was a great laser; however, my new Aesculight has many important features and improvements that were simply unavailable to me before!

Q: Could you describe the transition from your old Luxar to Aesculight?

A: The learning curve should be minimal for most surgeons. Of course, having twice the power entails having a certain experience and ability to utilize the laser at those higher wattages, but it's absolutely worth it for particular procedures. CO_2 laser surgery in general has a shorter learning curve (compared to Ultrasound and Endoscopy, for example), because with the laser 'what you see is what you get' in terms of tissue interaction…

Q: How did this enhanced cutting power affect your practice?

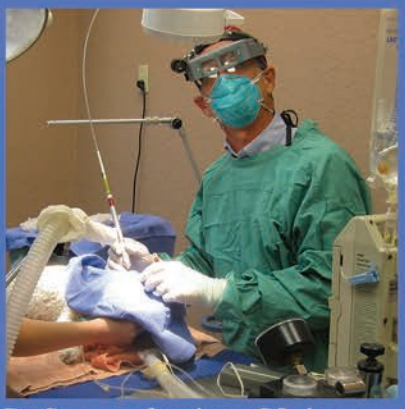
A: It's very important: having that capacity to achieve higher power settings is beneficial for procedures involving larger animals: areas like the back of the neck for larger dogs, areas which involve dealing with thicker skin… equine applications as well, certainly. So in other words – we are able to expedite and facilitate certain surgeries with the Aesculight that were otherwise more cumbersome and slower to perform with the older machine.

Q: How did the upgrade to the higher power laser system impact your practice financially?

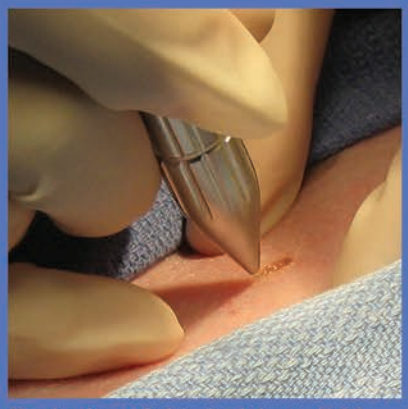
A: The upgrade in clinical value for my patients definitely coincides with my revenues from laser surgery going up from about $500 dollars per week to several thousand! The enhanced power and improved flexibility enables me to do more surgeries with greater speed, to cut through tissue much faster – cartilage is no problem, spays and neuters are achieved with a remarkably dry field, I appreciate the power density… in essence, client satisfaction is very high because of what I am able to do with the technology I have available. Of course, medical devices don't come cheap these days; however, if a veterinary practice has 2 doctors or more and has a surgical suite that's used 4 days a week, then the financial element of the decision is a no-brainer: they will be able to pay for the laser in under a year! My laser pays for itself…

Q: How important is the Adjustable Focal Spot Tipless Handpiece for your surgeries?

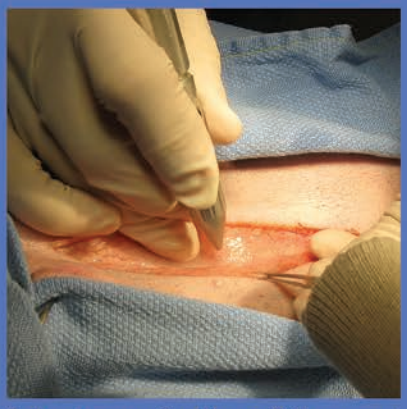
A: It's a totally new way of doing surgery. The tipless handle is a terrific way to adjust power density without changing the setting on the laser control panel. To be able to change between different spot sizes during surgery and then easily defocus at the same time - it's an absolute joy to use! It's also easier for the staff to clean and sterilize and we have no broken ceramic tips anymore! This handpiece literally pays for itself in terms of staff time: we save about $40-$50 a day, four times a week – the time and the expenses associated with taking care of tips. Laser tips are still a great way of doing surgery, don't get me wrong; it's just this Tipless handle is that much better!



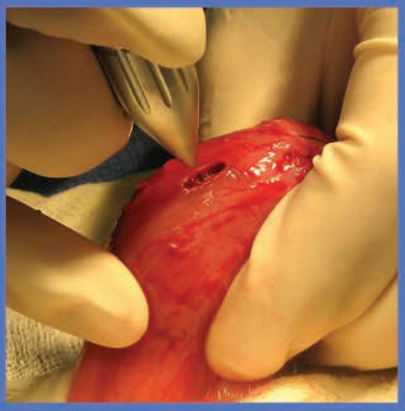
Dr. Sessa performing a CO_2 laser surgery.



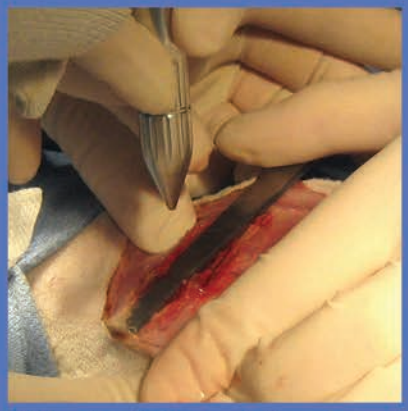
Beginning of skin incision – 0.25 mm spot size



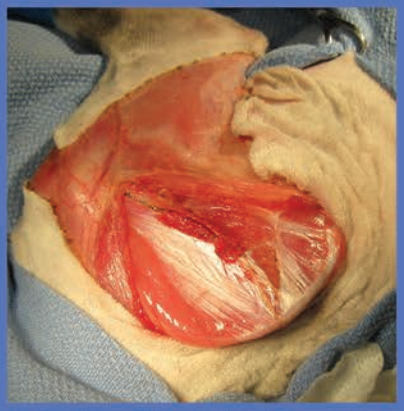
Subcutaneous incision – 0.4 mm spot size. Note the bloodless surgical field.



Cystotomy in progress – note excellent hemostasis.



Feline forelimb amputation - laser cutting muscle attachments.



Feline forelimb amputation - prior to removing the scapula.

Watch CO_2 laser surgery videos at www.Aesculight.com

About Dr. Sessa:

Dr. Paul Sessa earned his DVM from the University of California, Davis, in 1984. He practiced medicine in Escalon before joining the Veterinary Emergency Clinic in Modesto, Calif., in 1985. In 1990 he transferred to the Associated Veterinary Emergency Services Clinic in Stockton, Calif., while developing his Animal Home Health Mobile Care practice. Dr. Sessa now practices at Salida Veterinary Hospital in Salida, Calif.

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Quiz yourself on this issue's features

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1 **CONSULT THE EXPERT** PAGE 14
Which of the following plays a role in the emergence of infectious diseases in veterinary medicine?
A. Expanding vector ranges
B. Improved methods of detection
C. Antibiotic resistance
D. All of the above

2 **CASE IN POINT** PAGE 26
Which of the following is not true with regard to *Cryptococcus gatti* infection in cats?
A. The incubation period is variable and can be 1 to 12 months or longer.
B. Endemic areas include Canada and the Pacific Northwest region of the United States.
C. Immunocompetent cats can be infected.
D. It poses zoonotic risk to immunocompetent humans.

3 **PROCEDURES PRO** PAGE 31
Hair samples plucked for dermatophyte cultures are best collected from:
A. The periphery of lesions
B. The center of lesions
C. Nonlesional parts of the coat
D. All are equally adequate for sampling.

4 **TOP 5** PAGE 58
Hospital visitation dogs are at significantly elevated risk for *Clostridium difficile* shedding, which is likely acquired through:
A. Ingestion of contaminated raw diets
B. Immune suppression from stress of visitation
C. Ingestion of spores from hospital environment and patients
D. Coprophagy

5 **CONSULT THE EXPERTS** PAGE 65
Cobalamin supplementation should be instituted when serum levels fall below:
A. 250 ng/L
B. 350 ng/L
C. 450 ng/L
D. 550 ng/L

6 **CONSULT THE EXPERT** PAGE 68
Which of the following is not a potential consequence of anesthetic barotrauma?
A. Alveolar rupture
B. Open pneumothorax
C. Tension pneumothorax
D. Impaired venous return to the heart

1: D 2: D 3: A 4: C 5: A 6: B

POLLING PLACE

WE ASKED ...

Which protective measure against exposure to infectious disease is most difficult for you to maintain at your practice?

YOU ANSWERED ...

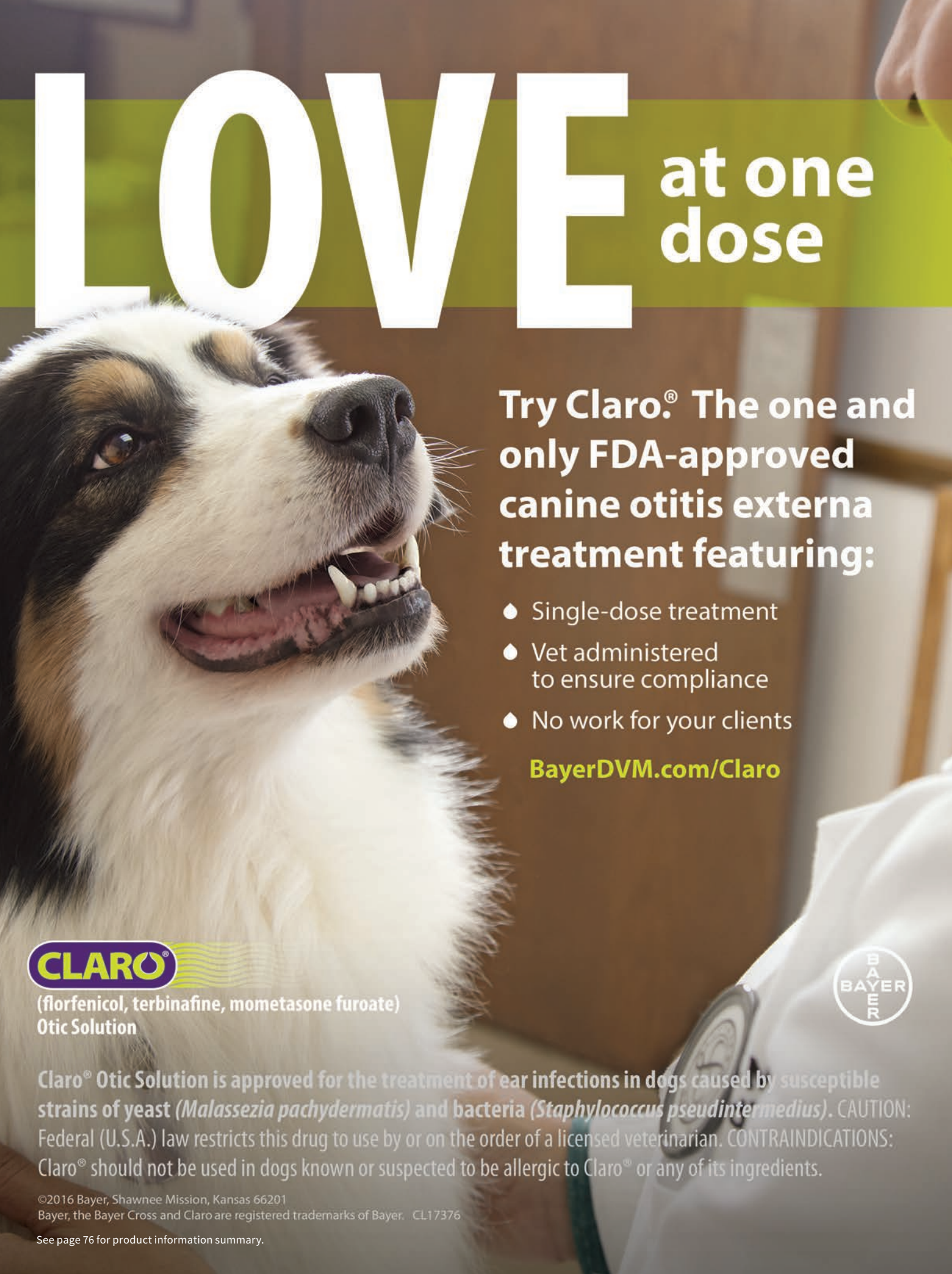
A. Isolating the infectious patient on presentation..... 52%
B. Disinfecting possibly contaminated areas..... 11%
C. Keeping up with laundry..... 8%
D. Enforcing self-protective measures among team members..... 29%

THIS MONTH'S QUESTION ...

Are fracture repairs performed at your practice?

A. No, we refer these cases.
B. We perform some pinning but no plating.
C. We perform all fracture repairs.

Go to cliniciansbrief.com to weigh in.



See page 76 for product information summary.

TRUST.

REWARD THEIR TRUST WITH THE HEARTWORM DISEASE PREVENTIVE THEY'LL LOVE

- PREVENTS HEARTWORM DISEASE
- TREATS AND CONTROLS 3 SPECIES OF HOOKWORMS
- TREATS AND CONTROLS 2 SPECIES OF ROUNDWORMS
- OWNERS PREFER IT[1] AND DOGS LOVE IT[2]
- SAFE FOR PUPPIES AS YOUNG AS 6 WEEKS OF AGE

[1] Data on file at Merial.
[2] Freedom of Information: NADA140-971 (January 15, 1993).

HEARTGARD Plus is a Merial product.
Merial is now part of Boehringer Ingelheim.

Boehringer Ingelheim

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

Heartgard® Plus (ivermectin/pyrantel)

See page 75 for product information summary.

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clinician's forum™
Expert Views from a Roundtable on Heartworm Prevention

Heartworm Prevention and Treatment

Clinical Recommendations in the Age of Resistance

Heartworm is an important parasite to prevent in dogs because of its life-threatening consequences. Yet, despite the broad availability and use of effective heartworm preventives and generally high awareness of the disease among dog owners, its incidence is increasing. Heartworm infection has now been diagnosed in dogs in all 50 states,[1] and according to the American Heartworm Society (AHS) 2016 Incidence Survey, the average number of positive cases per veterinary clinic rose by 21.7% over 2013 numbers.[1]

Macrocyclic lactones (MLs) are the only class of drugs approved for the prevention of canine heartworm disease, and veterinarians have been prescribing them for decades. An increase in lack of efficacy of MLs was first reported in 2004,[2,3] mainly in the Mississippi River Valley, with research confirming the existence of isolates of *Dirofilaria immitis* that are resistant to MLs presented in 2013.[4,5] Since then, additional resistant strains have been identified, with some strains outside the lower Delta region.[6-8] Recent survey work sponsored by AHS has further confirmed these findings through genetic analysis of microfilariae from field cases of dogs suspected of harboring ML-resistant *D. immitis*.[9] ***Figure 1*** (next page) is a composite showing 14 different individually identified isolates/strains resulting from the work of the above investigators.

The perception is that resistance is only a problem in the Mississippi Delta, but resistant strains can be found anywhere there are infected dogs.

—Dr. Susan Little

Infection with heartworm, whether due to ML-sensitive or ML-resistant strains, is now a nationwide concern with very simple risk factors. Heartworm disease can exist anywhere there are dogs, mosquitoes, and the potential for introducing infected dogs. At present, while ML resistance appears to be primarily concentrated in the Delta region, it is not understood how rapidly or how far it will spread. Today it is not unusual for dogs to travel with their families, and dogs are often transported to be rehomed following natural disasters from areas with high incidence of infection where resistant strains have

KEY POINTS

- All dogs should receive year-round heartworm preventives.
- All dogs should be screened for heartworm infection yearly with an antigen and a microfilariae test.
- Resistance to macrocyclic lactones has been shown to occur throughout the southeastern US.
- Despite resistance, macrocyclic lactones remain the mainstay of preventive treatment and are highly effective when used as prescribed.
- When prescribing a heartworm preventive, one should consider the ability of pet owners to comply with prescribed regimens and successfully administer medications.

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***D. immitis* isolates with confirmed resistance to MLs have been found as far north as Illinois and as far east as Alabama, with the majority of these isolates concentrated in the Mississippi Delta.**

—Dr. Tom McTier

been identified to areas where heartworm has been less frequently diagnosed. These factors, and others, create a situation where any dog is at risk—one that all clinicians need to be aware of and adjust their clinical practice to address. The AHS has issued a Heartworm Resistance statement acknowledging the confirmation of ML resistance with key points to discuss with pet owners.[10]

In the last 5 years, I have changed my approach to heartworm prevention because every dog in my clinic is at risk today. My clients don't know where the dog that lives next door traveled this year or if it was adopted from the Southeast US.

—Dr. Peter Eeg

This article summarizes a recent roundtable discussion among practicing veterinarians and veterinary parasitologists on how clinicians can best address these issues and actions they can take to provide the best protection for their patients.

Best Practices for Heartworm Prevention

The two main tenets of best clinical practice for preventing heartworm disease the roundtable experts identified are:

- Testing all dogs for heartworm antigen and microfilariae at least once a year, and
- Administration of an FDA-approved heartworm preventive medication, year-round, at the appropriate dose using a protocol designed for maximum compliance in the individual patient.

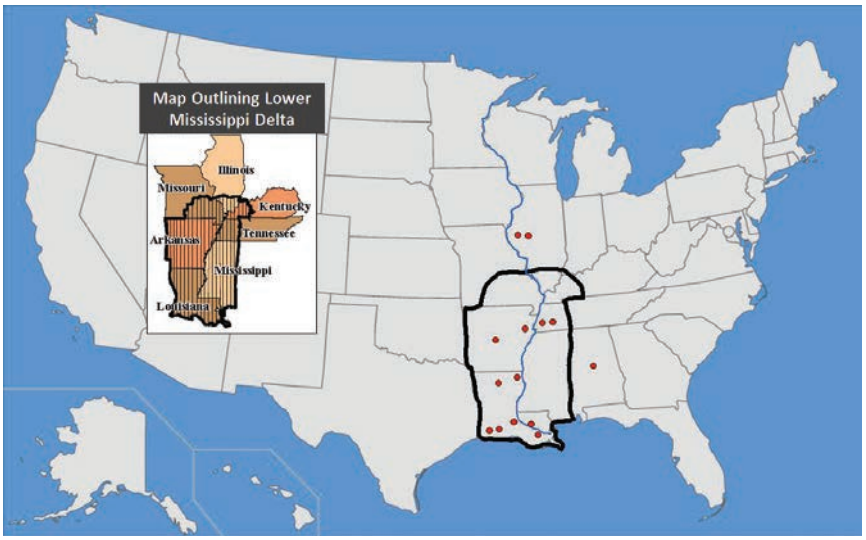
Year-Round Protection for Every Dog

Research has shown that a single heartworm-positive dog substantially increases the risk of infection for other healthy dogs in that neighborhood.[11] In an area where a large percentage of dogs are on prevention, an owner may be able to get away with no prevention or missed doses for a while because few of the mosquitoes in that area will be carrying heartworm. That should not deter us from emphasizing the importance of year-round prevention for all dogs.

—Dr. Peter Eeg

Veterinarians are strongly encouraged to adhere to the recommendations of the AHS[12] and the Companion Animal Parasite Council (CAPC).[13] Both groups recommend year-round protection, with no lapses, with an FDA-approved ML as well as limiting contact with mosquitoes. These drugs affect microfilariae, third and fourth-stage larvae, and in some instances of continuous use, adult heartworms.[7] Currently marketed preventives include:

- Oral, administered monthly by pet owner
  - Ivermectin
  - Milbemycin oxime
- Topical, administered monthly by pet owner
  - Moxidectin
  - Selamectin
- Injectable, administered every 6 months by veterinarian
  - Moxidectin



▲ **FIGURE 1** Location of confirmed or suspected ML-resistant heartworm isolates/strains. Each dot indicated an individual isolate. *Map courtesy of Dr. Tom McTier.*

For information on specific products, many of which are combined with other agents to provide broad-spectrum efficacy against multiple parasites, consult the AHS and CAPC websites.[12,13]

Annual Testing: Looking for Heartworm Infection Means Looking for Microfilariae as well as Antigen

If you are not testing for heartworm, you won't find it and you will think you don't have it. We have to be testing for both antigen and microfilariae routinely. Until a client has a heartworm-positive dog, a lot of them really don't understand the devastation the disease causes. It's our job to educate them—it is what our clients *expect* from us.

—Dr. Chris Rehm

Annual testing is another essential component of heartworm prevention. Both AHS and CAPC recommend that all dogs, including those on heartworm prevention, be tested annually using both antigen (Ag) and microfilariae (Mf) tests starting at 6 months of age. In some high-incidence areas, testing dogs twice each year may be indicated, particularly in dogs with high exposure to mosquitoes.

Both Ag and Mf testing is recommended because surveys have shown that some infected dogs can be Ag-positive and Mf-negative while others are Mf-positive and Ag-negative.

—Dr. Susan Little

Managing the Microfilaremic Dog

Understanding the life cycle of the heartworm (***Figure 2***, next page) is key to understanding heartworm treatment protocols. Melarsomine dihydrochloride, the only drug approved by the FDA for heartworm treatment, eliminates adult heartworms but does not kill larval stages. Therefore, after melarsomine (adulticide) treatment, dogs should be continued on ML preventives to kill these immature stages.[12,13] Topical moxidectin is the only drug with a label claim for the removal of circulating Mf in heartworm- positive dogs; other MLs have been used off label to clear Mf. No adverse events were seen in the studies conducted to secure FDA label approval of topical moxidectin for clearing Mf. If reactions are a concern in dogs with high numbers of circulating Mf, pretreatment with antihistamines and glucocorticosteroids can help minimize risk.[12]

Persistent circulating microfilariae must be eliminated because they serve as a means of presenting mosquitoes with a population of Mf that have been preselected for resistance by surviving the killing of the susceptible Mf with MLs.

—Dr. Dwight Bowman

Microfilariae can persist in infected dogs for more than a year after adults have been cleared,[12] even in the presence of very high levels of some MLs. In addition, a heartworm-positive dog may harbor heartworms ranging from <1 month to as long as 7 years. The wide range in maturity of heartworms in an infected dog can make it difficult to eliminate all stages of the parasite. A clinician may think a dog has been successfully treated only to find continued infection with adult heartworms or with Mf when retesting 6 or 12 months later. This needs to be a consideration when choosing a treatment protocol. Eliminating Mf at the beginning of treatment, initiating a 30-day course of doxycycline (to eliminate *Wolbachia*, a gram-negative bacteria found within the heartworm), providing continuous ML prevention (monthly or sustained-release moxidectin injectable), followed by a three-dose melarsomine protocol gives the highest probability of achieving heartworm-free status in the affected dog.[12] Delaying the start of adulticide treatment can allow additional pathology to develop in the patient.

Heartworm Resistance: the Threat to Our Patients is Here to Stay

The perception that resistance is only a problem in some areas of the South may stem in part from the fact that we are not screening to the same degree in other regions.

—Dr. Susan Little

Reported cases of loss of efficacy (LOE) of heartworm preventives were first published in the US in 2005,[2] with a heavy concentration in the Mississippi River Valley and Southeast region, and have persisted since then. Many of these cases were attributed to lack of full compliance with preventive regimens.[3] However, ML

BEST PRACTICE—PERFORM *BOTH* ANTIGEN AND MICROFILARIAE TESTING AT LEAST ONCE A YEAR

- **Antigen Tests**
  - Antigen tests detect antigen from the adult female heartworm.
  - Several good options are available for in-house testing, or samples can be sent out to a lab.
  - False-negative results can occur when infections are light, female worms are still immature, only male worms are present, test instructions have not been followed correctly, or Ag is blocked due to immune complexes.
  - Heat pretreatment of serum samples breaks down Ag-antibody complexes that can cause false-negative results,[14-18] but this approach is not recommended for routine use on all samples tested in clinical practice.
- **Microfilariae Tests**

  Microfilariae may be identified microscopically by several methods:
  - The modified Knott procedure, a concentration technique, is the preferred screening test with the most accurate results.
  - Examination of a wet mount of fresh blood or blood treated with an anticoagulant is a quick and easy option, although less sensitive than the Knott test.
  - Examining the buffy coat (liquid-cell interface) in a micro-hematocrit tube, looking for movement, is another method.
  - Concentration using a stained or unstained Millipore filter (now available from Amazon) is an additional option.
  - *D. immitis* Mf must be differentiated from those of *Acanthocheilonema (*formerly *Dipetalonema) reconditum* and, rarely in the US, from other *Dirofilaria* spp found in fresh blood samples.

Some veterinarians I talk to underestimate the threat in their local area. That may be due, in part, to the fact that they are not specifically looking for resistant strains when they have a heartworm-positive dog; they are more likely to presume it is due to a lack of compliance.

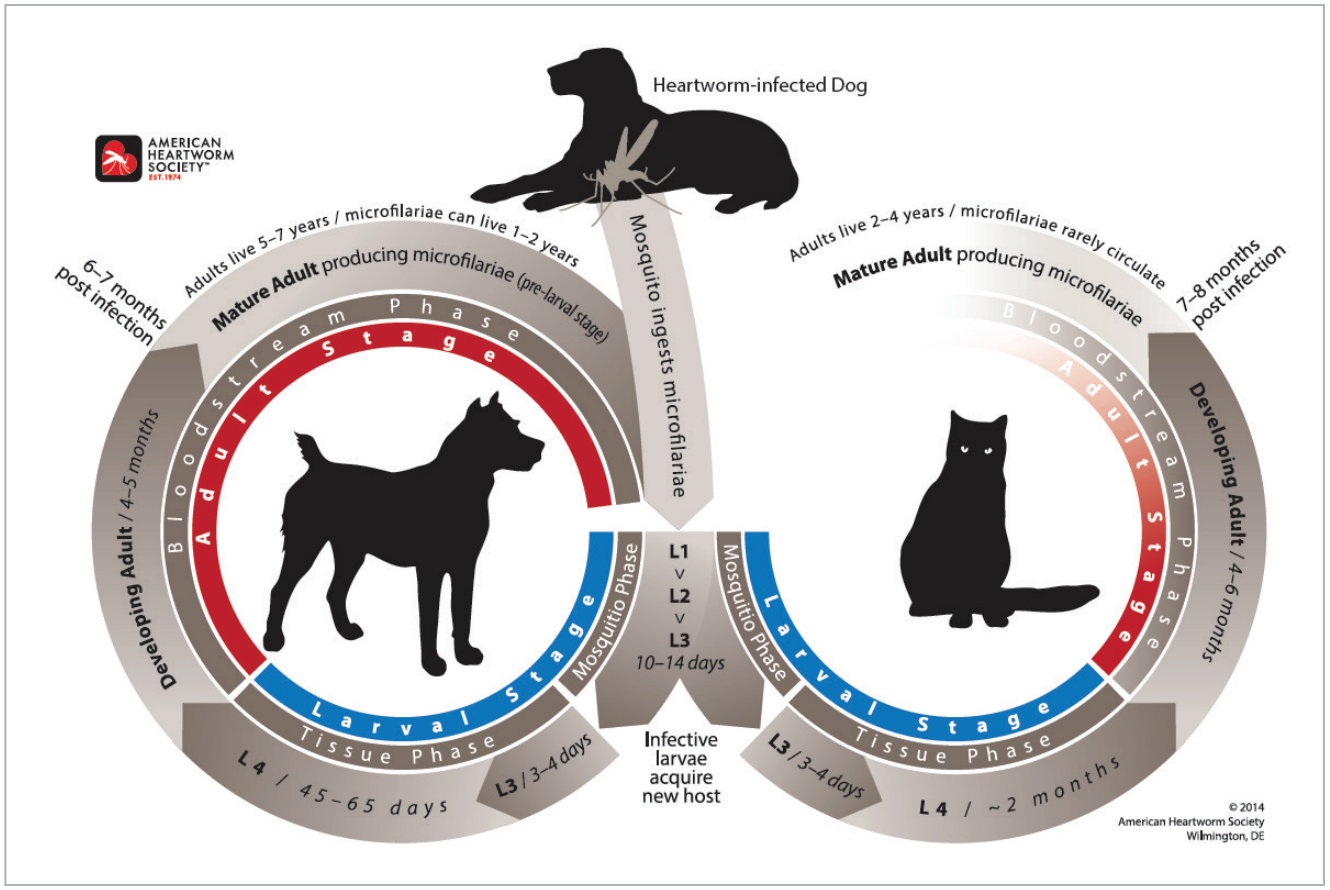
—Dr. Tom McTier

resistance has been confirmed in cases with well-documented compliance with preventives.[4,5] Whole genome analysis has been performed on isolates with documented LOE to identify genetic markers that correlate with evidence of resistance.[15]

There's no question that resistance is real; we have the scientific data to support that.[5] Multiple isolates have been identified—such as JYD-34 originally isolated from a dog in Illinois,[6] Yazoo-2013 from a dog in Mississippi, and Metairie-2014 isolated from a dog in Louisiana. Yet some veterinarians I talk to underestimate the threat in their local area. That may be due, in part, to the fact that they are not specifically looking for resistant strains when they have a heartworm-positive dog; they are more likely to presume it is due to a lack of compliance.

—Dr. Tom McTier

A complete review of the causes of ML resistance in heartworms is beyond the scope of this article, but contributing factors could include improper use of MLs (eg, using "slow kill" protocols, poor compliance leaving gaps in protection, not looking for Mf), as well as the parasite's natural adaptation to the drugs over time. Macrocyclic lactones remain the only effective FDA-approved class of drug currently available to prevent heartworm disease. Preserving efficacy of



▲ **FIGURE 2** The heartworm life cycle. Reprinted with permission from the American Heartworm Society.

MLs is of paramount importance in veterinary medicine.

It is very important that as a profession we use macrocyclic lactones appropriately and at the right doses if they are going to retain their efficacy to prevent canine heartworm disease.

—Dr. Dwight Bowman

Definitive diagnosis of suspected drug-resistant heartworm cases is not possible in the clinic due to the lack of point-of-care clinical tests or validated laboratory tests for detecting resistance in heartworms. Currently, the only means available to prove resistance is to perform a controlled efficacy study in a laboratory,[4,5] a time-consuming and expensive process that is not practical in clinical practice. The microfilariae suppression test (MFST), which measures Mf levels both before and after a microfilaricidal dose of ML, was first proposed by Geary and colleagues as a means for detecting resistance.[20] An algorithm utilizing the MFST to help clinicians evaluate cases of suspected resistance to MLs was recently reported.[21] Suspect blood samples can be sent to Dr. Cassan Pulaski at Louisiana State University (cpulaski@vetmail.lsu.edu) for further laboratory analysis. Samples then undergo screening by the team at McGill University to confirm the presence of genes believed to be related to drug resistance.

Five Steps Clinicians Can Take to Manage the Risk of Resistance Today and Looking Forward

1. Consistently Test and Use the Correct Methods

As discussed earlier, all dogs should be tested annually for heartworm using both an Ag test and a Mf test.

Early detection and early treatment lead to better outcomes. People have gotten the message with other chronic diseases; we need them to get the message with heartworm. Dogs should be re-tested every year because we know that some dogs become infected despite the fact that they were given a preventive.

—Dr. Susan Little

2. Use the Right Preventive Product for Each Patient and Owner

There is no cookie cutter parasite control protocol for all clients. Veterinarians should talk to each client about their lifestyle and their pet's lifestyle before choosing a medication.

—Dr. Lynn Buzhardt

Factors in selection of a heartworm preventive include compliance (see below), cost, convenience, and safety. Not all preventives have equal efficacy; some, like moxidectin in a sustained-release injectable formulation (ProHeart® 6, Zoetis) or in a high dose topical formulation, may be effective immediately while some other monthly products require three successive doses before they are fully effective, depending on the specific strain to which the dogs are exposed. Evaluate the prescribing information for each product, available online from the manufacturer, before making your selection.

3. Select Preventives for Your Practice—and Your Patients—That Increase Compliance

The one to pick is the product the client is able to consistently give and that covers the parasites that they're worried about.

—Dr. Andy Moorhead

We all have clients we assume are perfect in their compliance—only to find out they aren't!

—Dr. Chris Adolph

If we solve the compliance issue, we solve 98% of our heartworm infection problems.

—Dr. Byron Blagburn

Compliance has long been a problem in heartworm prevention, with no reliable way to confirm whether preventives purchased are actually administered at home by the owner. The consensus among practicing veterinarians in this roundtable was that use of injectable moxidectin increases compliance because it puts control back in the veterinary clinic, rather than having to rely on the pet owner remembering to treat the dog on time, all the time. The product provides 6 months of protection in a single dose and

BEST PRACTICE: MINIMIZING HEARTWORM TRANSMISSION BY RELOCATED DOGS

I see a lot of rescue dogs coming up from the South in my practice in Maryland. We immediately take a blood sample and test for microfilariae because they are very often heartworm positive. The rescue groups usually are only using an antigen test. If positive for Mf, we follow the AHS protocol and monitor them as closely as we can.

—Dr. Peter Eeg

Transporting and relocating dogs is an increasingly common practice—for example, during emergencies, such as hurricanes, when homeless dogs from heartworm-endemic areas in the southern US are transported to other areas to be rehomed. The AHS and Association of Shelter Veterinarians (ASV) have developed a protocol to minimize the risk of heartworm transmission in these cases,[19] which stipulates both Ag and Mf testing before transport. Some shelters and rescue groups may only do Ag testing, especially in a crisis situation. Clinicians treating these dogs upon arrival should first test for Mf, as Ag-negative, Mf-positive dogs are more common than previously thought.

It is important to obtain as much history as possible on relocated dogs regarding drugs used in past heartworm prevention and treatment. For example, some dogs may have received incomplete heartworm treatment, or been treated with levamisole to clear Mf that were not cleared with MLs.

If we solve the compliance issue, we solve 98% of our heartworm infection problems.

—Dr. Byron Blagburn

Broad-spectrum preventives are great if the owner gives them consistently, but we want to make sure the dog gets 6 months of heartworm medication and the injection will guarantee that.

—Dr. Lynn Buzhardt

can only by be administered by veterinarians and veterinary staff certified to do so.

Injectable moxidectin brings clients in more frequently, at least twice a year. I also think it protects the pet better overall, and takes away the compliance issue. I have seen no adverse reactions of any import.

—Dr. Peter Eeg

In parasite discussions with clients, we prioritize heartworms because they are the parasite most likely to kill the dog. Broad-spectrum preventives are great if the owner gives them consistently, but we want to make sure the dog gets 6 months of heartworm medication and the injection will guarantee that. If clients see a flea or tick, they'll remember to give medication, but there's no visible reminder with heartworm.

—Dr. Lynn Buzhardt

The fact that the owner must bring the dog back for a second visit in 5 to 7 months for the next 6-month dose benefits the patient by ensuring year-round protection and brings peace of mind to the owner who doesn't have to remember to give a monthly dose. A further benefit is that moxidectin has demonstrated efficacy against a resistant heartworm isolate.[22]

Moxidectin, the molecule itself, is the most potent ML preventive against *Dirofilaria immitis*. In the original studies of the oral formulation (available outside the US), moxidectin was 100% effective in preventing heartworm disease, providing complete efficacy at lower doses and for longer durations than other oral MLs.[23] This should be a factor in making optimal decisions about parasite control.

—Dr. Tom McTier

4. Communication—EVERYONE in the Practice Must Send the Same Simple Message

A clear and consistent message about heartworm prevention and screening is crucial. Resources are available to help educate pet owners about the importance of heartworm prevention, including clinic scripts for better communication about heartworm, on the AHS website (heartwormsociety.org). It is critical that the entire staff is on board. Below are some helpful tips from the panel to help improve client communications in your clinic.

Compliance is always going to be one of our biggest challenges, but we can improve it with good communication. We send an email, or sometimes a snail mail or a text, to remind our clients when their pets are due for parasite prevention and testing. We then follow up with a phone call or two if needed. The way we get them back is by making sure that we lead off our parasite discussion with heartworms.

—Dr. Cassan Pulaski

Keeping everyone in the practice on the same page, with the same talking points, is really important. Have three different people repeat one simple concise message and clients are more likely to retain the important parts when they leave.

—Dr. Lynn Buzhardt

Instead of going into the exam room and asking the client what they are using for flea and heartworm preven-

tion, ask when is the last time they gave heartworm and flea prevention, and *then* ask what they gave. That changes their answers and can open the all-important compliance discussion.

—Dr. Cassan Pulaski

5. Provide Protocols to Cover All Parasite Needs

If we prioritize heartworm as the most life-threatening parasite for the dog, we want to improve compliance for that particular parasite first. Then we can structure our protocol for control of other harmful parasites from that starting point.

—Dr. Lynn Buzhardt

Many of the ML preventives feature broad-spectrum coverage against a variety of other internal and external parasites, such as hookworms, roundworms, whipworms, and mange mites. Detailed information is available for each product at the CAPC website in the Quick Product Reference Guide.[13] Depending on the ML you choose, you'll need to put together a plan for protection from other parasites that are concerns for an individual patient.

For example, injectable moxidectin protects against hookworms (*Ancylostoma caninum, Uncinaria stenocephala)* in addition to the L3 and L4 stages of *D. immitis*. If roundworms (*Toxocara canis, Toxascaris leonina*) are an issue, you'll need to add pyrantel pamoate. If whipworms (*Trichuris vulpis*) are a problem, fenbendazole can be added to the regimen.

One thing we consider is potential for zoonotic disease transmission. When we choose a parasiticide protocol in Louisiana, it has to include roundworm and hookworm prevention to protect not only the pet but also the pet's family.

—Dr. Lynn Buzhardt

Best Practice: The New Clincal Standard Set Out By The Experts

- Year-round heartworm protection should be the standard for all dogs.
  - Heartworm is now found in all 50 states, so all dogs are at risk.
  - Use the right preventive product for each patient and their owner.
  - Choose a product that is likely to increase compliance to enhance prevention.
  - Despite resistance, MLs are still highly effective when used properly.
  - Make a plan for protection from other parasites to supplement the heartworm preventive selected for each patient.
- Perform annual screening tests.
  - Conduct both an Ag test and a Mf test.
  - Test twice a year in endemic areas where risk is high.
- Follow AHS and CAPC recommended protocols to treat heartworm infection.
  - Monitor for and treat persistent circulating Mf.
  - Send suspect blood samples for further laboratory analysis.

Injectable moxidectin brings clients in more frequently, at least twice a year. I also think it protects the pet better overall

—Dr. Peter Eeg

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