**CLINICAL FOCUS**

The Benefits of Chiropractic Care

Farm Sanctuary, a farm animal rescue organization based in California, acquired Regina, a Suffolk cross sheep, in late 2016. Two days after she arrived, Regina’s right hind leg was amputated at the University of California, Davis, Large Animal Clinic because the limb had been broken in 3 places shortly after birth and was left untreated by her previous owners. The surgery saved Regina’s life, but walking on 3 legs resulted in gait issues that threatened to cause significant back pain as she matured. The prescribed solution? Monthly chiropractic adjustments.

Jamie Peyton, DVM, DACVECC, chief of the Small Animal Integrative Medicine Service at UC Davis Veterinary Medical Teaching Hospital, examined Regina’s left hind leg in March 2017.

(continued on page 26)

CVC

Fear-Based Aggression in Dogs

At the 2017 Central Veterinary Conference in Virginia Beach, Virginia, veterinarian behaviorist John Ciribassi, DVM, DACVB, discussed fear-based aggression in dogs. He described body postures associated with fear-based aggression, when this type of aggression is most likely to occur, and appropriate management options.

Dr. Ciribassi noted that about 80% of the cases he sees are aggression based, and that canine aggression is not necessarily problematic or abnormal. Aggressive behaviors, he said, are normal tools dogs use in a variety of situations, such as for self-defense, acquiring food, defending resources, and establishing a pack structure.

(continued on page 21)

**SPECIAL FEATURE**

Repair Surgery Among Latest Treatments for Mitral Valve Disease

By Kim Campbell Thornton

Degenerative mitral valve disease (MVD) is the most common heart problem seen in dogs and typically affects small dogs aged 10 years and older.

In most cases, the disease is managed medically, but Michele Borgarelli, DVM, PhD, DECVM-CA, who lectured on the topic at the American College of Veterinary Internal Medicine (ACVIM) Forum in National Harbor, Maryland in June, says an upcoming ACVIM consensus statement on the treatment of MVD is forthcoming.

(continued on page 22)

**WVC**

Managing Cats With Upper Respiratory Infection

If you see cats in your practice, you undoubtedly will see a significant number of upper respiratory infections, according to Mike Lappin, DVM, PhD, DACVIM, a professor in the Department of Clinical Sciences at Colorado State University. This is in large part because most adopted cats come from an animal shelter, which are an ideal environment for the spread of infectious organisms.

Dr. Lappin discussed the leading causes of respiratory infections in cats—bacterial and viral—in a presentation at the 2017 Western Veterinary Conference in Las Vegas.

The International Society for Companion Animal Infectious Diseases (ISCAID) developed guidelines for the...

(continued on page 16)

**WVC**

Pain Control for the Aging Horse

Medical advances mean that many horses are living longer, sometimes up to 35 years. As they age, horses may be prone to developing painful disease states.

At the 2017 Western Veterinary Conference in Las Vegas, Lori Bidwell, DVM, DACVA, CVA, CVTP, presented an update on analgesia in geriatric horses. “Geriatric” is defined as having achieved 75% of the average lifespan. The average lifespan of horses...
Clients want to fight fleas and ticks – not their dogs.

Protect dogs with the beef-flavored chew they love.¹

⁰Data on file at Merial.

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IMPORTANT SAFETY INFORMATION: NexGard® Chewables is for use in dogs only. The most frequently reported adverse reactions included pruritus, vomiting, dry/flaky skin, diarrhea, lethargy, and lack of appetite. The safe use of NexGard in pregnant, breeding, or lactating dogs has not been evaluated. Use with caution in dogs with a history of seizures. For more information, see full prescribing information or visit www.NexGardForDogs.com.
CAUTION: Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.

Description:
NexGard® (afoxolaner) is a chewable tablet that contains 2 mg of afoxolaner, an acaricide and insecticide. NexGard is available in four sizes: 11.3, 28.3, 68, or 136 mg afoxolaner. Each chewable is formulated to provide a minimum afoxolaner dosage of 1.14 mg/lb (2.5 mg/kg). Afoxolaner has the chemical composition C19H18Cl2F3N2O2 (2,2-trifluoro-1-(2-methylpropan-2-yl)ethan-1-one).

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

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

Dosing Schedule:

<table>
<thead>
<tr>
<th>Body Weight</th>
<th>Afoxolaner Per Chewable (mg)</th>
<th>Chewables Administered</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.0 to 7.0 lbs</td>
<td>11.3</td>
<td>One</td>
</tr>
<tr>
<td>7.1 to 14.0 lbs</td>
<td>19.5</td>
<td>Two</td>
</tr>
<tr>
<td>14.1 to 28.0 lbs</td>
<td>58</td>
<td>One</td>
</tr>
<tr>
<td>28.1 to 60.0 lbs</td>
<td>135</td>
<td>One</td>
</tr>
</tbody>
</table>

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

Flea Treatment and Prevention:
Treatment with NexGard may begin at any time of the year. In areas where fleas are common year-round, monthly treatment with NexGard should continue the entire year without interruption. To minimize the likelihood of flea reinfection, it is important to treat all animals within a household with an approved flea control product.

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

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

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

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

Adverse Reactions:
In a well-controlled US field study, which included a total of 333 households and 475 treated dogs (415 administered afoxolaner, 200 administered active control), no serious adverse reactions were observed with NexGard.

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

Table 1: Dogs With Adverse Reactions.

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Afoxolaner</th>
<th>Scal acaride control</th>
</tr>
</thead>
<tbody>
<tr>
<td>N1 % (n=415)</td>
<td>N2 % (n=200)</td>
<td></td>
</tr>
<tr>
<td>Vomiting with and without food</td>
<td>17</td>
<td>4.1</td>
</tr>
<tr>
<td>Diarrhea (mild)</td>
<td>13</td>
<td>3.1</td>
</tr>
<tr>
<td>Diarrhea (moderate)</td>
<td>13</td>
<td>3.1</td>
</tr>
<tr>
<td>Lethargy</td>
<td>7</td>
<td>1.6</td>
</tr>
<tr>
<td>Anorexia</td>
<td>5</td>
<td>1.2</td>
</tr>
</tbody>
</table>

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

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

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

To report suspected adverse events, for technical assistance or to obtain a copy of the MSDS, contact Merial at 1-888-637-4251 or www.merial.com/NexGard. For additional information about adverse drug experience reporting for animal dogs, contact FDA at 1-888-FDA-1480 or online at http://www.fda.gov/AnimalVet/SafetyHealth.

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

Effectiveness:
In a well-controlled laboratory study, NexGard began to kill fleas four hours after initial administration and demonstrated ≥96% effectiveness at eight hours. In a separate well-controlled laboratory study, NexGard demonstrated 100% effectiveness against adult fleas 24 hours post-infestation for 36 days, and 58% effective at 12 hours post-infestation through Day 21, and on Day 28. In a 28-day 30 ng/kg NexGard was 81.1% effective 12 hours post-infestation. Dogs in both the treated and control groups were infested with fleas on Day 1—generated flea eggs at 12- and 24-hour post-treatment (D.7 eggs and D.7-17 eggs in the NexGard treated dogs, and D.10 eggs and D.11-17 eggs in the control dogs at 12- and 24-hours, respectively). At subsequent evaluations post-infestation, fleas from dogs in the treated group were essentially unable to produce any eggs (D.7 eggs) while fleas from dogs in the control group continued to produce eggs (D.7-11 eggs). In a 90-day US field study conducted in households with existing flea infestations of varying severity, the effectiveness of NexGard against fleas on the Day 30, 60 and 90 visits compared with baseline was 98.0%, 99.7%, and 99.9%, respectively.

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

In well-controlled laboratory studies, NexGard demonstrated ≥96% effectiveness against Dermacentor variabilis, ≥94% effectiveness against lice, 94% effectiveness against Rhipicephalus sanguineus, and 88% effectiveness against Pyrethrin-resistant adult Ixodes scapularis, 48 hours post-infestation for 30 days. At 72 hours post-infestation, NexGard demonstrated ≥96% effectiveness against Amblyomma americanum for 30 days.

Animal Safety:
In a 90-day safety study, NexGard was administered orally to six to 8-week-old Beagle puppies at 1, 3, and 5 times the maximum exposure dose (63.6 mg/kg) for three treatments every 28 days, followed by three treatments every 14 days, for a total of six treatments. Dosage in the control group were sham-dosed. There were no clinically relevant effects related to treatment with NexGard, body weight, food consumption, clinical pathology (hematology, clinical chemistry, or coagulation tests), gross pathology, histopathology or organ weights. Vomiting occurred throughout the study, with a similar incidence in the treated and control groups, including one dog in the 5x group that vomited four hours after treatment. In a well-controlled field study, NexGard was used concomitantly with other medications, such as vaccines, anthelmintics, antibiotics (including topical), steroids, NSAIDS, anesthetics, and antihistamines. No adverse reactions were obtained from the concurrent use of NexGard with other medications.

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

Dosage Schedule:
NexGard is available in four sizes of beef-flavored soft chewables: 11.3, 28.3, 68 or 136 mg afoxolaner. Each chewable size is available in color-coded packages of 1, 3, or 6 Beef-flavored chewables. NARDI 141, Approved by FDA.

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KEEPING UP WITH YOUR EDUCATION

Continuing education conferences abound in veterinary medicine. Whether you are a veterinarian or team member, work in a private practice or a shelter, teach students or are a student, there is a conference for you. In fact, hundreds of conferences are held throughout the country each year on every topic imaginable.

Attending veterinary conferences (conventions, symposia, meetings, forums, academies) is an invaluable learning experience that keeps veterinary professionals up-to-date on the latest and greatest in veterinary science and medicine, from cutting-edge diagnostics and therapeutics to refreshers on dealing with common clinical conditions. Conference attendance not only allows you to get out of the practice—or classroom, zoo, office, or wherever you happen to work—and learn about best practices and changing protocols, but it also affords the opportunity to network with like-minded colleagues, explore every possible avenue of veterinary practice, and learn what new products are available.

Many private practitioners count themselves lucky if they get the opportunity to attend or send their team members to a single conference each year. For others, a number of factors make conference attendance all but impossible. After all, attending conferences comes at a cost, whether that’s the time away from the practice and your clients or the registration and travel expenses. That’s where American Veterinarian® comes in. Our mission is to provide you with clinical updates and information that will help you improve patient outcomes and positively affect the way you practice. One of the primary ways we do that is by bringing you news and information from conferences nationwide. This year, we’re covering nearly 15 national, regional, and local conferences. In this issue alone we feature 4 of them—Western Veterinary Conference, Central Veterinary Conference, American Animal Hospital Association Conference, and American College of Veterinary Internal Medicine Forum—with topics that range from canine behavior and biosecurity to pain control in horses and respiratory infection in cats, among others. And we continue our extensive coverage on our website, so check out AmericanVeterinarian.com/conferences for more useful clinical information from a host of experts in academia and practice.

We understand that veterinary medicine is constantly evolving and to provide the best care possible for your patients, you must educate yourself continually. We’re proud to help you in that endeavor through comprehensive conference coverage in every issue.

Happy reading!

Mike Hennessy, Sr
Chairman and CEO
For more clinical research, news, conference updates, and video expert advice, visit AmericanVeterinarian.com.
SPECIAL FEATURE

22
Repair Surgery Among Latest Treatments for Mitral Valve Disease

By Kim Campbell Thornton

We highlight exciting new and upcoming advances in the treatment of the most common heart disease in dogs, plus a pet owner’s account of her dog’s reparative surgery.

CONFERENCE COVERAGE

AAHA
12
Analysis of Pleural, Peritoneal Fluid
Dr. Mike Scott discusses the importance of sample handling, transport, and analysis.

WVC
16
Managing Cats With Upper Respiratory Infection
Dr. Mike Lappin outlines 2 of the 3 leading causes of respiratory infection in cats.

ACVIM
20
Chemotherapy-Induced Vomiting and Inappetence
Which chemotherapeutics do veterinary oncologists avoid, and what drugs do they prescribe for common adverse effects in their cancer patients?

CVC
21
Fear-Based Aggression in Dogs
Dr. John Ciribassi outlines when fear-based aggression is most likely to occur, plus how to identify and manage it.

VETERINARY WORLD NEWS

8
Dogs and Reading Performance in Austrian Children
Humoral Response to Leptospirosis Vaccination in Horses

9
Which States Have the Plumpest Pets?
Declawing Cats: Adverse Medical and Behavioral Outcomes

10
Poverty, Dog Ownership, and Canine Rabies Vaccination in Uganda
Canine Mammary Tumors: Predicting Malignancy Using Ultrasonography

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CLINICAL FOCUS

ALTERNATIVE MEDICINE
26
The Benefits of Chiropractic Care
These treatments are used to address a wide variety of health issues in animals, and more veterinarians are choosing them.

NEUROLOGY
28
Can Sleep Improve Memory in Dogs?
Hungarian researchers studied whether sleep has the same memory consolidation effect in dogs as it does in humans.

INFECTIOUS DISEASES
30
Eliminating Canine Rabies From the Western Hemisphere
Much progress has been made in eradicating this deadly disease, but roadblocks remain, say experts.

DEPARTMENTS

MAKING A DIFFERENCE
32
Helping Those Who Cannot Help Themselves
A chance encounter with a homeless man and his dog leads one veterinarian to start a unique charity.

PRODUCT SPOTLIGHT
34
A look at some of the latest and greatest products in veterinary medicine.
REVOLUTIONARY!
The first diagnostic tool for early screening and monitoring of diabetes in felines and canines.

Start Screening Now!
A1Care (HbA1c) is an easy, accurate and cost-effective veterinary mail-in diabetes test for the early screening, diagnosis and long-term monitoring of canine and feline diabetes. Pre-screen at-risk populations: overweight, senior and pre-disposed breeds.

With a few drops of dried blood, A1Care determines the average blood glucose levels for the previous 70 days in felines and 110 days in canines thus scoring the patient as normal, pre-diabetic or diabetic.

<table>
<thead>
<tr>
<th>A1c (HbA1c) Levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average/Normal</td>
</tr>
<tr>
<td>Feline 1.8</td>
</tr>
<tr>
<td>Canine 3.3</td>
</tr>
</tbody>
</table>

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800-213-1439
info@baycomdiagnostics.com
Dogs and Reading Performance in Austrian Children

By JoAnna Pendergrass, DVM

Previous studies have reported numerous ways in which dogs positively affect learning in children, including reducing stress, improving concentration, and enhancing social interaction. Given these positive effects, reading programs have increasingly incorporated dogs into their curricula. To date, however, reading-with-dog programs are not widespread in German-speaking countries, such as Austria.

For the current study, researchers evaluated whether dogs would have an immediate effect on the reading performances of 36 Austrian children with below-average reading skills. Each child underwent 2 testing sessions (TS1, TS2) spaced 1 week apart; a dog was present in 1 session and absent in the other. During each test session, children performed 2 reading tests: a standardized test assessing sentence and text comprehension and a nonstandardized repeating reading (RR) test evaluating reading speed and short-term improvement. For the RR test, children twice read an age-appropriate section of text out loud.

Researchers measured several physiologic variables. Saliva samples were collected throughout the test sessions for cortisol measurement, and the children also wore a heart rate (HR) belt and watch for HR measurement. Behavioral variables—talking, nervous movements, self-manipulation—were also evaluated. Self-manipulation behaviors included scratching and nail chewing.

In TS1, cortisol levels were not affected by a dog’s presence. However, in TS2, the levels were higher with a dog’s presence than its absence; this contrasts with previous studies in which a dog’s presence had a calming effect. As for HR, between test sessions, this measure was higher with a dog’s presence. Interestingly, within test sessions, mean HRs for children with and without a dog were not significantly different. In addition, in TS1, children with a dog made fewer nervous movements and talked less yet had similar amounts of self-manipulation, compared with children without a dog. And in TS2, children with a dog engaged in more self-manipulation but had similar levels of nervous movements and talking as children without a dog.

Overall, reading performances were better in TS2 than TS1 for the standardized reading test and better in TS1 than TS2 for the RR test. In each testing session for both tests, reading performances did not significantly improve with a dog’s presence compared with its absence. Interestingly, though, for the RR test in TS1, having a dog present improved reading performance from the first to the second reading. Researchers concluded that “repeated sessions with the dog are crucial to achieve substantial effects on reading performance.” The researchers concluded that a dog’s presence had little influence on a child’s reading performance and various physiologic and behavioral parameters. The observed improvements in reading performance and increases in other parameters with a dog’s presence may have been due to activation of the appetitive system, which promotes reward-seeking behaviors.

Unlike previous studies on dog-assisted reading, in which a child’s reading skills were either normal or not assessed, this study evaluated children with below-average reading skills. Given this different study population, “results produced new information, which is important for understanding the underlying mechanisms and conditions of an effective pedagogical intervention to improve reading skills with the support of dogs.”


Humoral Response to Leptospirosis Vaccination in Horses

By Laurie Anne Walden, DVM, ELS

Leptospirosis vaccination significantly affects anti-Leptospira antibody production in horses, say the authors of a new study. Although the humoral response was short-lived and was not apparently increased by booster vaccination, the investigators consider vaccination to be an important component of equine leptospirosis control.

Horses’ humoral responses to leptospirosis vaccines are not well understood, say the authors of the study, which was conducted in Brazil. They note that 1 equine multivalent leptospirosis vaccine is available in Brazil. (In the United States, the only leptospirosis vaccine currently licensed for use in horses is a monovalent vaccine against L. pomona.)

The study included 54 mares with no history of leptospirosis vaccination and no signs of uveitis. Thirty-six mares randomly assigned to the vaccination group received 2 doses of multivalent leptospirosis vaccine on days 0 and 40. Eighteen mares in the control group received no vaccination.

To identify natural infection, the investigators tested a random sample of 30 mares (15 in each group) on day 0 with urinary polymerase chain reaction testing. Tests from 2 mares in each group were positive, showing that they were renal carriers of leptospirosis.

The researchers conducted microscopic agglutination tests to detect humoral responses to specific Leptospira serovars. On day 0, 26 of 54 mares were seroreactive, with no significant different between groups. Seroreactivity in these mares was to L. australis and L. icterohaemorrhagiae.

By day 7, the percentage of seroreactive mares in the vaccination group had increased from 44.5% to 94.4%, and tests detected antigens to all 11 serovars included in the vaccine. This increase persisted for most serovars until day 60. The increase in the number of seroreactive horses was sustained to day 90 only for L. copenhageni, L. icterohaemorrhagiae, and L. pyogenes.

In the control group, the percentage of seroreactive mares also significantly increased by day 7, although the increase was smaller (55.6% to 66.7%). By day 90, there was no significant difference in overall seroreactivity between the groups. However, anti-Leptospira antibody titers were higher in vaccinated mares than in unvaccinated mares throughout the study.

The investigators used enzyme-linked immunosorbent assay to identify immunoglobulin classes (IgG and IgM) in the mares’ serum. On day 0, the mares with Leptospira antibodies had a much higher concentration of circulating IgG than IgM, which the authors note is consistent with natural exposure. There was no significant difference between groups on day 0. In vaccinated mares, IgM increased relative to IgG over time. Both IgG and IgM were higher in vaccinated mares than in unvaccinated mares. By day 90, concentrations of both IgG and IgM had dropped in both groups.

An unexpected result was that booster vaccination (day 40) did not increase the number of seroreactive horses. Previous studies of leptospirosis vaccination in dogs, pigs, and cattle have shown the opposite effect, say the authors.

The authors note that the largest humoral responses were to serovars already present in the herd on day 0, suggesting that vaccination may have a booster effect. They add that different responses to different serovars is a limitation of multivalent vaccines.

Declawing Cats: Adverse Medical and Behavioral Outcomes

By JoAnna Pendergrass, DVM

A retrospective study published in the Journal of Feline Medicine and Surgery reported that declawed cats have an increased risk for back pain and behavioral problems. Such results, the authors wrote, should prompt further questioning of the practice of declawing in the United States.

Onychectomy is a common feline surgical procedure in the United States and Canada. In fact, nearly 25% of pet cats in the United States are declawed. The surgery is indicated not only to eliminate destructive behaviors but also to treat medical issues, like nail bed cancer. Many professional veterinary organizations, such as the American Association of Feline Practitioners and the American Veterinary Medical Association, recommend onychectomy only after behavioral modification is unsuccessful. Several studies have reported postoperative morbidities associated with onychectomy, including lameness, nail regrowth, and chewing at the digits. To date, onychectomy’s long-term consequences remain unknown.

The authors evaluated 274 cats (137 each, declawed and nondeclawed); 176 were client-owned cats and 98 lived in animal shelters. All cats received a physical examination during which they were assessed for back pain and barbering. The cats’ medical histories of the past 2 years also were reviewed for surgical declaw technique and documented adverse behaviors (biting, aggression, and periuria/perichezia).

Declawed limbs were radiographed, and the images were evaluated for residual fragments of the third phalanx (P3), bone remodeling of the second phalanx (P2), and interdigital osteoarthritis. Declawed digits were categorized according to percentage of residual P3.

A surprisingly high percentage of declawed cats (63%) had radiographic evidence of residual P3, reflecting “the use of poor or inappropriate surgical techniques,” the authors wrote. P2 bone remodeling was radiographically evident in 8% of declawed cats; whether this remodeling resulted from the surgical technique used or was a consequence of P3 removal was unknown.

Overall, compared with nondeclawed cats, declawed cats had significantly higher odds of back pain and each of the adverse behaviors. The odds of back pain, aggression, and barbering were about 3 times higher in declawed cats than in nondeclawed cats. Unexpectedly, the odds of back pain and barbering were significantly higher in shelter cats than in client-owned cats, independent of declaw status; the authors suspected this may have been due to more frequent observations and reporting by shelter staff.

The authors also found that, compared with nondeclawed cats, declawed cats with residual P3 had significantly higher odds of back pain and adverse behaviors. Notably, declawed cats with residual P3 were nearly 10 times more likely to demonstrate periuria/perichezia. If declawed cats have painful phalanges, the authors wrote, they may prefer eliminating on a soft substrate rather than digging in gravel-like litter. In addition, compared with nondeclawed cats, declawed cats with no residual P3 had significantly higher odds of biting and periuria/perichezia. This indicates that, even with optimal surgical technique, declawed cats still have an increased risk for behavioral problems.

When comparing the impact of residual P3 in only the declawed cats, the authors observed that the odds of back pain, periuria/perichezia, and aggression were significantly higher in cats with than without residual P3. The authors noted that this was the first reported observation of an association between residual P3 and back pain in declawed cats.

The authors concluded that despite the potential biases of observational and retrospective studies, the “substantial and statistically significant” odds ratios in the present study provide clear evidence of an association between declawing and adverse medical and behavioral outcomes in cats.


Which States Have the Plumpest Pets?

By Kaitlynn Ely

It seems pudgy pets are everywhere today. In its 2017 State of Pet Health Report, Banfield Pet Hospital noted that over the past 10 years, obesity rates in pets have increased by an average of nearly 164%. One in 3 cats and dogs today are overweight. In its report, Banfield ranked each state based on the average weight of its cats and dogs.

The findings were based on a survey in which Banfield veterinarians nationwide were asked about the percentages of overweight dogs and cats that visited their practice. Included in this study were 2.5 million dogs and 500,000 cats.

Interestingly, there does not seem to be a strong correlation between obesity in humans and their furry friends. For example, while Minnesota’s pets are the fattest in the nation, the state has a relatively low percentage of obese adults (26%), ranking it 37th according to The State of Obesity Project, a collaborative effort between the Trust for America’s Health and the Robert Wood Johnson Foundation. Likewise, Nebraska ranks second in pet obesity but 14th in human obesity, with 31.4% of the adult population being obese. And while Louisiana is the fattest state in America for humans (36.2%), only 21% of dogs and 25% of cats in the state are overweight.


Poverty, Dog Ownership, and Canine Rabies Vaccination in Uganda

By JoAnna Pendergrass, DVM

Rabies is a global health threat that kills almost 60,000 people per year, with approximately 19,000 of these deaths occurring in sub-Saharan Africa. Although the canine rabies virus variant has been eliminated from most developing countries, it remains prevalent in sub-Saharan Africa. Rabies intervention programs have been unsuccessful and rabies surveillance is lacking across Africa, particularly in Uganda. Without adequate surveillance, risk models have been developed to estimate human and animal rabies burden. However, these models have not considered dog ecology and are not country-specific.

Results from a knowledge, attitudes, and practices (KAP) survey conducted in Uganda in 2013 revealed that poverty level heavily influences dog ownership and canine rabies vaccination coverage in the country. This study, according to the researchers, “represents one of the most comprehensive attempts to characterize the dog population and rabies risk in Uganda.”

Researchers conducted the 65-question KAP survey in 24 Ugandan villages. Results were analyzed at the household level (size of household, owned livestock value, level of dog care provided) and village level (population density, poverty). Using statistical models, the researchers also estimated the population of owned dogs, canine rabies vaccination coverage, and human rabies risk.

In the 24 villages, 798 households representing 4375 people completed the survey. Of these households, 13% owned dogs. Overall, the total number of owned dogs was 175, making the human:dog ratio 25:1. Nearly 60% of the owned dogs had a previous rabies vaccination. This rate, although surprisingly high, was still below the threshold for effective herd immunity (70%) and was heavily influenced by poverty level. The average village poverty level was 45%—higher than Uganda’s national average of 38%. The most common reasons for a dog being unvaccinated were lack of rabies vaccine access and no government vaccination, likely reflecting that vaccine availability is limited to Uganda’s periodic national vaccination campaigns. Notably, these reasons were given only in the areas where poverty is highest.

The researchers determined that human population density and poverty level significantly affected estimates of Uganda’s owned dog population and canine rabies vaccination rate. Adjusted for poverty, the human:dog ratio of 25:1 nearly doubled to 47:1 and the 57% rabies vaccination rate dropped to 35.4%.

A modeled estimate indicated that 90% of Ugandans live in areas where enzootic rabies transmission could occur. “The findings from this study,” the authors wrote, “should be used to enhance current mass canine rabies vaccination strategies in Uganda through the strategic use of resources where they will have the greatest impact.”

For the future, the authors advised further validation of this study’s modeled estimates. These estimates, they noted, can guide rabies vaccination strategies but should not replace routine rabies surveillance.

Canine Mammary Tumors: Predicting Malignancy Using Ultrasonography

By Laurie Anne Walden, DVM, ELS

Researchers in Brazil have found that acoustic radiation force impulse (ARFI) elastography can be an effective predictor of malignancy in canine mammary tumors. “Several reports have demonstrated the applicability and limitations of B-mode ultrasonography, Doppler, elastography, and contrast-enhanced ultrasonography (CEUS) in the evaluation of breast cancer in humans and canines,” the authors wrote. “However, no report has yet compared the efficacy of these ultrasound techniques in predicting malignancy of mammary tumors.”

The prospective study included 300 mammary masses from 153 client-owned dogs seen at the veterinary teaching hospital at Universidade Estadual Paulista, São Paulo, from 2014 to 2016. A veterinary sonographer evaluated the tumors with each of the 4 techniques before the dogs underwent mastectomy. Definitive diagnoses were made with histopathology after mass excision. Of the 300 tumors, 246 (82%) were classified as malignant and 54 (18%) were classified as benign on histopathology.

B-mode (conventional) ultrasonography reveals a tumor’s size, margins, echogenicity, echotexture, and invasiveness. The sensitivity, specificity, and accuracy of certain tumor dimensions measured by this technique were judged moderate for predicting malignancy. For other tumor characteristics, this technique was not effective in differentiating malignant from benign masses. In this study, malignant tumors were larger than benign tumors on B-mode ultrasonography.

Doppler color flow imaging assesses a tumor’s blood supply. Spectral Doppler vascular indexes can help distinguish malignant from benign mammary masses in humans, say the authors. In this study, published in PLOS ONE, vascular indexes measured by Doppler ultrasonography had moderate sensitivity, specificity, and accuracy for predicting malignancy in canine mammary tumors.

CEUS was performed after intravenous administration of sulfur hexafluoride contrast material. This technique allows visualization of smaller blood vessels than can be seen with color Doppler imaging, and the degree of contrast enhancement is considered an indicator of malignancy or benignity in humans. In this study, although CEUS revealed macro- and microcapillarization of tumors, none of the measured parameters correlated significantly with malignancy. The authors judged the sensitivity of this technique to be high but the specificity to be low for predicting malignancy.

Elastography is a relatively new technique that measures the deformability of a mass (the elasticity vs rigidity of the tissue). Mammary carcinomas are more rigid than benign masses because of increased stromal collagen levels, say the authors. In this study, ARFI elastography characteristics were similar to those previously reported in humans and dogs. The mean shear wave velocity measured by this technique was 95% accurate in predicting malignancy.

ARFI elastography is “an exceptionally effective technique for malignancy prediction in canine mammary masses,” the authors wrote. “Based on the results from this study, quantitative ARFI elastography proved to be the best method of ultrasonographic prediction of malignancy in mammary masses.” They recommend ARFI elastography as a rapid, noninvasive method of predicting mammary mass malignancy in dogs.
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0517-595-I01B
**Analysis of Pleural, Peritoneal Fluid**

By Karen Todd-Jenkins, VMD

(continued from front cover)

Transportation, and accurate fluid analysis at the American Animal Hospital Association (AAHA) Annual Conference in Nashville, Tennessee.

When a fluid sample is obtained from a patient and submitted for laboratory analysis, natural processes alter the character of the fluid’s components, making it difficult to ensure that the sample harvested from the patient has the same characteristics as the sample that arrives at the laboratory. For example, Dr. Scott noted that cell deterioration begins as soon as the sample is collected. Phagocytosis of contaminant bacteria can occur within minutes, and phagocytosis of erythrocytes can occur within hours. Microbes can also proliferate in the fluid before it can be analyzed at the diagnostic laboratory.

**SAMPLE HANDLING**

Some alterations in sample character are difficult to avoid, but careful handling can minimize the impact of these processes on diagnostic accuracy. Dr. Scott commented that the most common errors he sees involve inappropriate sample preparation and shipment. For example, failure to keep a sample at the proper temperature during shipment can affect sample quality.

“Fluids should be mailed to arrive overnight, and the package should be insulated and contain ice packs to limit cell deterioration. The sample itself should also be insulated from ice packs so it won’t freeze,” Dr. Scott said. He also recommends using an adequate technique to collect the fluid and, once the sample is obtained, submitting some of the fluid in an EDTA tube to hinder clotting of bloody or proteinaceous samples. Another aliquot can be collected into a regular tube with no clot activator or gel.

**SLIDE PREPARATION AND SUBMISSION**

To optimize testing accuracy, Dr. Scott advises preparing prepared slides with the fluid specimens that are submitted in the tubes. “We recommend sending cytologic preparations made from the fresh fluid so that cell appearance, as it was prior to any in vitro change, can be assessed,” he noted. At least 2 unstained smears should be submitted with each stained smear, and rigid slide holders should be used for shipment.

Making the correct slides for cytologic analysis depends on the nature of the fluid, Dr. Scott cautioned. Cloudy fluid can be used to make direct smears using the “wedge” technique many veterinarians and technicians employ to make blood smears.

<table>
<thead>
<tr>
<th>Percentage of Dogs with Abnormal Health Observations Reported in Clinical Field Study (2 mg/kg/day)</th>
<th>Observation</th>
<th>Carprofen (n=129)</th>
<th>Placebo (n=132)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inappetence</td>
<td>1.6</td>
<td>1.5</td>
<td></td>
</tr>
<tr>
<td>Vomiting</td>
<td>3.1</td>
<td>3.8</td>
<td></td>
</tr>
<tr>
<td>Diarrhea/Stool soft</td>
<td>3.1</td>
<td>4.5</td>
<td></td>
</tr>
<tr>
<td>Behavior change</td>
<td>0.8</td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td>Dermatitis</td>
<td>0.8</td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td>PU/PD</td>
<td>0.8</td>
<td>--</td>
<td></td>
</tr>
<tr>
<td>AST increase</td>
<td>7.8</td>
<td>8.3</td>
<td></td>
</tr>
<tr>
<td>ALT increase</td>
<td>5.3</td>
<td>5.4</td>
<td></td>
</tr>
<tr>
<td>BUN increase</td>
<td>3.1</td>
<td>3.5</td>
<td></td>
</tr>
<tr>
<td>Ketonuria</td>
<td>14.7</td>
<td>9.1</td>
<td></td>
</tr>
</tbody>
</table>

**Percentage of Dogs with Abnormal Health Observations Reported in Surgical Pain Field Studies with Caplets**

<table>
<thead>
<tr>
<th>Observation</th>
<th>Carprofen (n=46)</th>
<th>Placebo (n=49)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vomiting</td>
<td>10</td>
<td>13.4</td>
</tr>
<tr>
<td>Diarrhea/Stool soft</td>
<td>6.7</td>
<td>6.0</td>
</tr>
<tr>
<td>Urate disease</td>
<td>1.3</td>
<td>1.3</td>
</tr>
<tr>
<td>Dermatitis/Skin lesion</td>
<td>2.6</td>
<td>1.3</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>0.7</td>
<td>0.0</td>
</tr>
<tr>
<td>Apnea</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Oral/Periodontal disease</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Urinary tract disease</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Wound drainage</td>
<td>0.0</td>
<td>0.0</td>
</tr>
</tbody>
</table>

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

During investigational studies for the chewable tablet formulation, gastrointestinal signs were observed in some dogs. These signs included vomiting and soft stools.

Post-Approval Experience

Although not all adverse reactions are reported, the following adverse reactions are based on voluntary post-approval adverse drug experience reporting.

The categories of adverse reactions are listed in decreasing order of frequency by body system.

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

Hepatic: Inappetence, vomiting, jaundice, acute hepatic toxicity, hepatic enlargement, hyperbiliurbinemia, bilirubinuria, hyperbilirubinemia. Approximately one-fourth of hepatic reports were in Labrador Retrievers.

Neuologic: Ataxia, paroxysmal, paralytic, vestibular signs, disorientation.

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

Behavioral: Sedation, lethargy, hyperactivity, restless, aggressiveness.

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

Dermatologic: Pruritus, increased sweating, alopecia, pyrargyric moist dermatitis (hot spot), necrotizing pancreatitis, vasculitis, ventral ecchymosis.

Immunologic or hypersensitivity: Facial swelling, hives, erythema.

In rare situations, death has been associated with some of the adverse reactions listed above.

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However, if the fluid is clear, it is helpful to create a concentrated sample for slide preparation. To do this, place the fluid sample in a tube and spin it in a centrifuge (as if preparing a urine sample for analysis of sediment). Then, remove the supernatant, resuspend the sediment in the remaining fluid, and use the concentrated material at the bottom of the tube to make the slide.

Dr. Scott also described an alternate technique for slide preparation of concentrated material. “Another option is to make flowback (ie, line, stop-flow) preparations,” he said. “The procedure to make these starts as that for a direct smear, but when the spreader slide reaches about two-thirds of the way across the slide, stop the spreading and lift the spreader slide up to yield a straight edge rather than a feathered end to the smear. Then tip the slide vertically so that the fluid at the end of the smear flows back down toward the base. This concentrates cells and spreads them out.”

If a concentrated sample is created for submission of slides, that should be noted on the laboratory submission form. Otherwise, the cell smear findings may be misinterpreted by laboratory analysts.

SAMPLE PROCESSING
Minor sample processing errors can affect the accuracy of test results. “The impact may be minimal or substantial, an example of the latter being when cell deterioration interferes with recognition of atypical cell populations and prevents a diagnosis of neoplasia that should have been made,” Dr. Scott said. Although preparation and submission errors are common, it doesn’t necessarily mean the sample shouldn’t be used, as important information can still be obtained. However, it is worth the extra effort to follow best-practice recommendations.

Another problem area of the fluid analysis process relates to the terms used to classify and communicate about fluids. Dr. Scott cautioned that fluids are not classified or evaluated consistently in veterinary medicine. “People have often classified effusions as transudates or exudates based primarily on numeric values for protein and cell concentrations, and the cutoffs have varied. Samples in the numeric gray zones have often been called modified transudates.” However, he noted, “Exudates can have low or high protein or cell concentrations under various circumstances, effusions can have high cell concentrations but not be exudates, transudates can have low or moderate protein concentrations depending on their source, and many fluids classified as modified transudates are not transudates that became modified as the name implies. So, protein and cell concentrations do not necessarily reflect the pathogenesis of the fluid accumulation.”

Dr. Scott uses a classification approach that aligns the composition of effusions with their pathogenesis, as much as possible. This requires attention to microscopic findings, other patient findings, and knowledge of how effusions form. For example, although exudates typically have increased protein concentrations and higher nucleated cell concentrations (commonly predominated by neutrophils), if a patient is hypoproteinemic, it could have an exudate without a high protein concentration. Similarly, a septic exudate from a neutropenic patient may have lower nucleated cell and neutrophil concentrations than anticipated, but phagocytized bacteria would still indicate the presence of exudation and, therefore, inflammation. And high fluid cellularity predominated by atypical lymphocytes would reflect a neoplastic (lymphomatous) effusion, not an exudate.

But not all effusions have a clear pathogenesis. A peritoneal effusion with a low cell concentration (mixed macrophages, lymphocytes, and neutrophils) and a moderate protein concentration could be a proteinaceous exudate or a protein-rich transudate, so Dr. Scott would classify it nonspecifically as a proteinaceous effusion. If the patient was known to be in congestive heart failure, the findings would fit a protein-rich transudate caused by protein-rich fluid emanating from the liver. Dr. Scott advised consideration of these factors when classifying and interpreting fluid analysis findings.

CONCLUSION
Fluid analysis, including cytology, can be an invaluable tool. As with any diagnostic test, however, sample collection, processing, handling, and interpretation all play roles in the ultimate value of the result. Clinicians can improve the value of these tests by taking a few precautions during sample preparation and handling and interpreting the results in light of the patient’s condition. These minor changes can ultimately result in improved diagnostic accuracy and patient outcomes.
Does Your Practice’s Biosecurity Protocol Need a Tune-Up?

(continued from front cover)

Lucas Pantaleon, DVM, MS, DACVIM, MBA: Using standards of practice and other veterinary guidelines, veterinary teams already do things like systematic hand washing, use of personal protective equipment, and instrument sterilization. However, in the hubbub of a typical day at a veterinary facility, strict and effective cleaning and disinfection are elements of infection prevention and control that can be overlooked.

What’s the connection between disinfection protocols and biosecurity, and why are they so critically important?

The issue is larger than it may seem. I consider biosecurity in veterinary medicine part of the One Health concept, which involves multiple disciplines collaborating and learning from each other with the objective of putting things into practice to help keep humans, animals, and the environment safe and healthy.

With respect to infectious disease prevention or biosecurity, veterinarians and physicians think in similar terms, so infectious disease control should be thought of from a One Health perspective—not only in terms of learning from different disciplines but also understanding that some of the things our counterparts in human medicine do to prevent hospital-associated infections could be applied to veterinary medicine so we can learn from each other and collaborate for the benefit of everyone.

For example, 1 thing human hospitals do that veterinary practices could consider is the use of disinfecting wipes. Wipes are very prevalent in human health care. They’re being used in some veterinary practices, but I think their use is increasing and, in certain situations, [they] could be used more. For example, because of the high flow of patients coming through exam rooms, you need a disinfectant agent with a shorter contact time (ie, capable of killing microbes quickly) to clean between appointments. Another thing that veterinary practices don’t do a lot is high-level disinfection of semicritical devices, such as endoscopes or other types of devices that come in contact with mucous membranes. Sometimes we’re not as good as we should be at disinfecting those devices; that’s something that maybe we can learn from our colleagues in human health.

WHY STANDARDIZE DISINFECTION PROTOCOLS?

Why is it so important for a veterinary hospital to have a standardized disinfection protocol?

Aside from the issues of safety and biosecurity, cost is a consideration. Just 1 patient acquiring an infection while visiting the hospital often ends up costing more than using a state-of-the-art disinfectant and proper protocols for prevention of infectious diseases. In addition, the potential costs to clients should not be overlooked. Let’s take canine parvovirus and canine influenza as examples. Besides patient suffering and the emotional stress placed on families, clients could face significant treatment costs if their pet picks up either of these viruses at the hospital. Careful evaluation of disinfectants and implementation of proper cleaning and disinfection practices can prevent or minimize the likelihood of these kinds of infections and the added costs associated with treating them.

You mentioned parvovirus and influenza. Are these pathogens among the most difficult to eradicate?

There are many different classes of pathogens, and their risk for causing disease varies. Parvovirus is one that is concerning because it’s a very difficult pathogen to kill. It’s a nonenveloped virus and hence inherently more resistant to disinfectants. In contrast, influenza virus has an envelope membrane made of lipids, so it’s easier to disrupt with cleaners and disinfectants. Other pathogens that we worry about include the upper respiratory complex pathogens. They represent a mixed bag of bacteria, viruses, and mycoplasma, but they’re relatively easily killed by disinfectants.

How much of a concern is leptospirosis, and is it easily eradicated in a hospital?

There has been more talk recently about leptospirosis because its prevalence has increased. In terms of disinfecting, 1 good thing is that leptospirosis doesn’t survive very long in the environment. As long as the surface is dry and clean, the microorganism basically dies. It would persist for some time in water. In veterinary clinics, where surfaces are normally nonporous, using a hospital-grade disinfectant with an acidic pH will inactivate the bacteria in the environment.

Once a practice establishes a disinfection protocol, can the same protocol be used throughout the entire hospital?

No, because different areas of the hospital have different risks. For example, if you’re in a grooming area, you would assume that those animals are healthy for the most part. Similarly, you would hope that dogs coming into a boarding facility are required to be vaccinated and are generally healthy. So, the risks in those areas will be a little bit lower. However, you have to understand that a boarding facility is like a kindergarten; you have large populations of animals interacting and playing with each other—nose-to-nose contact, perhaps sharing the same toys, and the like. So, disease transmission would be easy there.

WHERE ARE WE NOW?

Most veterinary practices already have some disinfection practices in place. What are we missing?

Lucas Pantaleon, DVM, MS, DACVIM, MBA: Using standards of practice and other veterinary guidelines, veterinary teams already do things like systematic hand washing, use of personal protective equipment, and instrument sterilization. However, in the hubbub of a typical day at a veterinary facility, strict and effective cleaning and disinfection are elements of infection prevention and control that can be overlooked.

Proper cleaning and disinfection practices can prevent or minimize infections and the costs associated with them, said Dr. Pantaleon.
Each kind of disinfectant, whether it's a single active ingredient

Are disinfectants really all that different? If so, how?

These areas should be cleaned and disinfected differently.

for routine patient care, such as vaccination or yearly exams.

more risk in an isolation area than in an exam room that is used

in a hospital there is a higher risk for acquiring contagious
diseases due to the fact that sick animals share a common en-
vironment. Hospitalized animals can be immunocompromised,
making them more prone to acquiring an infectious disease
from surfaces. So, the level of cleaning and disinfecting in hos-

diagnostic disinfectant is able to kill specific pathogens at a certain

duct passes the test, the manufacturer can then claim that parti-
cular disinfectant is able to kill specific pathogens at a certain
contact time. So, manufacturers are regulated by the EPA re-
garding what they can say.

Do any of those products work better than others?

They all have different parameters. Some work better because
they have a broader spectrum and a faster contact time, so in
certain situations they can kill pathogens quickly when time is

critical. For example, quaternary ammoniums aren’t very good
for hard-to-kill (nonenveloped) viruses, like parvovirus, while
other agents, such as accelerated hydrogen peroxide, would
work well for those types of viruses. Bleach is readily inactivated
by organic material, so using products whose efficacy is less
affected by the presence of organic material would be ideal.

How are disinfectants tested and regulated? Are manufactur-
ers required to disclose specific information about efficacy?

In the United States, disinfectant products are tightly regulated
by the Environmental Protection Agency (EPA). The products
are put through very stringent tests in order to obtain the
label claim for each pathogen. Products are tested for efficacy
against specific pathogens at specific contact times. If the pro-
duct passes the test, the manufacturer can then claim that parti-
cular disinfectant is able to kill specific pathogens at a certain
contact time. So, manufacturers are regulated by the EPA re-
garding what they can say.

How important should safety be? And do we ever need
to trade safety for efficacy when considering which
disinfectants to use?

Safety is very important. Even today, products are still being
used that are not safe for people or animals and can cause
different side effects. Sometimes there are strong smells to be
concerned about, or the active ingredient can cause a skin
reaction if the worker comes in direct contact with it. So, I think
it’s important to understand what types of products are being
used, to use them properly, and to keep safety for animals,
humans, and the environment top of mind when using some
of these products. That should be paramount. An effective
disinfectant doesn’t have to be harmful because now we have
technologies that don’t have to be harmful to kill the pathogens.
So, you have to try to select products that use newer tech-
nologies and are safer.

If you think about accelerated hydrogen peroxide, that parti-
cular product has a very high safety profile and a very high
killing rate for pathogens. So, we don’t need to use something
harmful to be able to kill pathogens.

Which products are safest for the environment?

When I think about something that is environmentally safe, I
would say the accelerated hydrogen peroxide products are a
good example. Accelerated hydrogen peroxide does not have
residual activity and is safe for the environment because it de-
grades into water and oxygen. Furthermore, the surfactants in
the accelerated hydrogen peroxide formulation are considered
environmentally friendly.

Looking Ahead

What challenges are on the horizon for veterinary practices
in this area?

I think people are taking biosecurity and infectious disease
control seriously, and awareness continuous to grow. Regard-
ing disinfectants, many veterinary practices select a product
based on price and not on efficacy or safety. Sometimes practices
don’t have someone in charge of infectious disease prevention with
the knowledge to do that type of job. We all know that veterinarians are busy and that’s
understandable, but unfortunately, they some-
times don’t really want to be the leaders or have
time to understand more about biosecurity and
why it’s important.

Biosecurity is an extremely important com-
ponent of patient care. To that end, infectious
disease prevention should be 1 of the things we do
every day in order to provide the best care for our patients. Further, not
only can choosing the right disinfectant help ensure the over-
all success of a biosecurity program, but it can have a posi-
tive and dramatic impact on facility maintenance costs and
employee health. Veterinary practices should also understand
that the entire veterinary team has a role in implementing
disinfection procedures, so commitment from the top down is
necessary for success.

| TABLE. Common Disinfectants Used by Veterinary and Medical Facilities |
|----------------|----------------|----------------|
| PRODUCT        | ADVANTAGES     | POTENTIAL DISADVANTAGES |
| Chlorine (bleach) | Broad efficacy | Unstable, health hazards, poor cleaner |
| Alcohol         | Safe           | Slow acting, poor cleaner |
| Phenolics       | Kill tuberculosis | Health hazards |
| Biguanides      | Broad efficacy | Human and environmental health hazards |
| Aldehydes       | Broad efficacy | Human and environmental health hazards |
| Hydrogen peroxide | Safe, sustainable | Unstable |
| Organic acids   | Safe, sustainable | Limited efficacy |
| Quaternary ammonium | Broad efficacy, safe | Slow acting |
| Peracetic acid  | Fast acting    | Health hazards |
| Accelerated hydrogen peroxide | Broad efficacy, fast acting, safe, sustainable | Gloves and goggles recommended for handling concentrated solution |

Infectious disease prevention should be 1 of the things we do every day in order to provide the best care for our patients.
(continued from front cover)
treatment of respiratory disease that are available at iscaid.org. The guidelines are available to anyone, and Dr. Lappin encouraged all attendees to become familiar with them.

**BACTERIAL CAUSES**

Determining whether a patient has a bacterial component to its upper respiratory disease is difficult. The ISCAID guidelines state that all cats with signs of purulent or mucopurulent ocular discharge, nasal discharge, conjunctivitis, sneezing, and epistaxis may have a bacterial component to their disease. They also define acute infections as those lasting less than 10 days and chronic infections as lasting longer than 10 days.

Dr. Lappin reminded attendees that secondary bacterial infections associated with feline herpesvirus (FHV-1) or feline calicivirus (FCV) are more common than primary bacterial infection. Secondary bacterial organisms often include *Pasteurella multocida*, *Staphylococcus* spp, *Streptococcus* spp, *Escherichia coli*, and anaerobes. Primary causes of bacterial infection include *Bordetella bronchiseptica*, *Chlamydia felis*, *Mycoplasma* spp, *Streptococcus* spp, and *P. multocida*.

For cats with signs of upper respiratory tract disease of less than 10 days’ duration, taking a careful history is an important part of evaluating potential causes, which can include vaccination, exposure to other cats, foreign bodies, contacts with a shelter or veterinary hospital, exposure to dogs, and stress. A thorough physical exam to check for lower respiratory issues and a feline leukemia virus/feline immunodeficiency virus test to check immune status are in order.

According to the ISCAID Working Group, there is limited benefit to performing cytology to ascertain an upper respiratory infection’s bacterial component. Culture and sensitivity testing is also not encouraged in acute cases because common bacterial pathogens are difficult to grow in standard cultures and a positive culture may be the result of commensal bacterial growth. In acute cases with no other identified problems, ISCAID recommends observation for 10 days because the cause may be an uncomplicated viral infection that should resolve on its own.

For suspected cases of secondary bacterial rhinitis, veterinarians are encouraged to do a workup if problems or clinical signs persist or worsen after 10 days. Dr. Lappin reminded the audience that rhinitis could be secondary to trauma, tooth problems, polyps, soft palate issues, cancer, foreign bodies, and viral-induced inflammation. Patients that present acutely and are not getting better on their own or with or without antibiotics (in cases that originally presented with a fever) should be worked up for these other causes. If the workup yields no evidence of another disease in chronic cases, ISCAID recommends choosing an antibiotic based on culture and sensitivity results and continuing its use 1 week beyond the resolution of clinical signs.

**VIRAL CAUSES**

Viral diseases are thought to be the most frequent cause of upper respiratory illness in cats. In the majority of cases, the cause is FHV-1 or FCV. If oral lesions are present, think FHV-1, but if you see oral ulcers, think FCV. Chronic stomatitis, uveitis, and facial dermatitis have also been associated with FHV-1.

Viral rhinitis can recur several times with or without a bacterial component. Treatment with oral Lysine at 250 to 500 mg twice daily may be helpful in the management of FHV-1-associated illness, but only at the full dose. Lysine, either alone or in fortified food, however, has not demonstrated any effectiveness in preventing recurrence of FHV-1. Ayclovir is an antiviral used for treating herpes outbreaks in humans. However, it is toxic to cats and should be avoided. Famciclovir is relatively safe in cats and can be used at a dose of 40 to 90 mg/kg orally every 8 to 12 hours. Cidofovir is a topical agent that can be used twice daily to treat ocular FHV-1; it is more convenient, appears to cause less irritation than other ocular therapies (eg, idoxuridine), and is available through some compounding pharmacies. Giving oral human interferon daily may help some cats chronically infected with FCV or FHV-1 through immunomodulation. Human interferon is available through specialty pharmacies.

The use of Nestlé Purina’s Fortiflora (*Enterococcus faecium* SF68) in normal cats increases the percentage of T-helper cells in blood.2 The probiotic was also shown to decrease conjunctival scores in one group versus controls.3

In 1 study, a single-dose intranasal FHV-1/FCV modified-live vaccine given to shelter cats that failed to improve with supportive and antibiotic treatment had some benefit.4 The vaccine appeared to be more effective than repeated doses of alpha or beta interferons. Interestingly, some of the cats dropped out of the study, as moving them from the shelter into a fostering environment improved their clinical signs sufficiently to exclude them from the study. This indicates the role stress plays in recrudescence of viral illness and suggests that modulating stress may be a key treatment component with FHV-1 or FCV-infected cats. The results of another study of an intranasal modified-live vaccine showed a decrease in sickness compared with controls, perhaps indicating an increased local immune response 7 days after challenge with *B. bronchiseptica*.5

In Dr. Lappin’s patients that respond to intranasal vaccination, he will repeat the vaccine up to 3 times per year.

Dr. Lappin pointed out that respiratory viral pathogens are ubiquitous in animal shelters, and cats that spend 23 days in a shelterlike environment have a 98% chance of being exposed to FHV-1 or FCV. Exposure does not mean fulminant illness, however, and many clinical cases involve young, old, immunocompromised, or stressed cats. Adapting shelters and homes to the social and environmental needs of cats and using stress reducers, such as the synthetic feline pheromone Feliway, can help reduce the number and severity of feline viral upper respiratory outbreaks.

References available at AmericanVeterinarian.com.
A flavorful way to fight feline dermatophytosis*

- One and only** FDA-approved treatment
- Cherry-caramel liquid formulation
- Cost-effective¹, safe and easy to administer
- Convenient pulse therapy

*Caused by Microsporum canis.
**Only FDA-approved systemic treatment currently in market.

Contact your Elanco sales representative for more information today!

ITRAFUNGOL oral solution is indicated for the treatment of dermatophytosis caused by Microsporum canis in cats.

Important Safety Information

Do not administer to cats with hypersensitivity to itraconazole. ITRAFUNGOL has not been shown to be safe in pregnant cats and should only be used in pregnant or lactating cats when the benefits outweigh the potential risks. Not for use in humans. Keep this and all medications out of reach of children. Wash hands and exposed skin after use. Use with caution in cats with renal dysfunction or impaired liver function. If clinical signs suggestive of liver dysfunction develop, treatment should be discontinued. ITRAFUNGOL is a cytochrome p-450 inhibitor and may increase or prolong plasma concentrations of other drugs metabolized by this pathway. Cats suffering from heart disease should be carefully monitored during treatment. The most common adverse reactions reported in clinical trials include vomiting, diarrhea, decreased appetite and elevated hepatic enzymes. Please see Brief Summary of Prescribing Information on page 18.

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(itraconazole oral solution)

10 mg/ml
Antifungal for oral use in cats only

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

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

Indication:
ITRAFUNGOL oral solution is indicated for the treatment of dermatophytosis caused by Microsporum canis in cats.

Dosage and Administration:
The solution should be administered orally using the enclosed graduated dosing syringe.

The daily dosage is 5 mg/kg (0.5 mL/kg) body weight administered once daily on alternating weeks for 3 treatment cycles. Cats are treated during weeks 1, 3, and 5, and left untreated during weeks 2 and 4.

See product insert for complete dosing and administration information.

Contraindications:
Do not administer to cats with hypersensitivity to itraconazole.

Warnings:

ITRAFUNGOL (itraconazole oral solution) has not been shown to be safe in pregnant cats (see Animal Safety section). ITRAFUNGOL should only be used in pregnant or lactating cats when the benefits outweigh the potential risks.

User Safety Warnings:
Not for use in humans. Keep this and all medications out of reach of children. Wash hands and exposed skin after use. In case of accidental contact with eyes, rinse thoroughly with water. In case of pain or irritation, seek medical advice. In case of accidental ingestion, rinse mouth with water and seek medical advice.

Special precautions for person administering the veterinary product to the animal:
Microsporum canis dermatophytosis is a zoonotic disease (a disease that can be transmitted from animals to humans); therefore consult a physician if a suspected lesion occurs on a human. Wear protective gloves when handling the animal during treatment or when cleaning the syringe. Wash hands and exposed skin after handling the animal.

ITRAFUNGOL has not been shown to be sporocidal; therefore in order to reduce zoonotic potential, environmental contamination, and to decrease course of the disease, topical and environmental treatment should also be utilized.

Precautions:
ITRAFUNGOL has been associated with renal changes found on histopathology that were not noted after an eight week recovery period. Use with caution in cats with renal dysfunction.

ITRAFUNGOL is metabolized by the liver (mainly CYP3A) and can cause elevated liver enzymes. Use with caution in cats with impaired liver function. If clinical signs suggestive of liver dysfunction develop, treatment should be discontinued.

ITRAFUNGOL is a cytochrome P-450 inhibitor and may increase or prolong plasma concentrations of other drugs metabolized by this pathway, such as amitriptyline, amiodarone, benzodiazepines, bupropion, cisapride, corticosteroids, cyclosporine, ivermectin, and macrolide antibiotics.

Negative inotropic effects have been reported in literature when itraconazole was administered intravenously to dogs and healthy human volunteers. Cats suffering from heart disease should be carefully monitored during treatment.

Adverse Reactions:
In the laboratory effectiveness study, adverse reactions related to exposure to ITRAFUNGOL were primarily related to the gastrointestinal tract. Two ITRAFUNGOL-treated cats experienced transient hypersalivation during the dosing period. Vomiting was observed in 5 ITRAFUNGOL-treated cats (12.5%) during the dosing period compared to four cats (10%) in the control group. Diarrhea was observed in 9 ITRAFUNGOL-treated cats (22.5%) during the dosing period as compared to 7 cats (17.5%) in the control group. One ITRAFUNGOL-treated cat showed mild increases in alanine aminotransferase (ALT) and aspartate aminotransferase (AST) at the end of the dosing period. No related clinical signs were observed, and these values returned to normal by the end of the follow-up period. One cat in the ITRAFUNGOL-treated group was noted to have lid erythema and lid induration once during the study.

Field safety was evaluated in 266 cats randomized to receive itraconazole oral solution. Of the 266 cats that received at least one dose of itraconazole oral solution, adverse reactions included 35 cases (13%) of one or more elevated hepatic enzymes and 6 cases (3%) of gastrointestinal upset, including decreased appetite, vomiting and/or diarrhea. Other infrequent adverse reactions included less than 5 cases each of somnolence, depression, and increased salivation.

For technical assistance or to report suspected adverse drug events, contact Elanco Animal Health at 1-888-545-5973.

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

Effectiveness:

Laboratory Study
Effectiveness was demonstrated using ITRAFUNGOL (itraconazole oral solution) in a masked, placebo controlled laboratory study. Eighty cats were experimentally infected with Microsporum canis and treated with either ITRAFUNGOL or sterile water (control product) for the proposed therapeutic treatment schedule followed by a 4-week follow-up period. No topical therapy was used during this study. A statistical difference (P = 0.0003) in mycological cure rate (defined as two consecutive negative mycological cultures) was demonstrated between cats treated with ITRAFUNGOL (24/40 or 60%) versus control (11/40 or 27.5%). Ninety percent of ITRAFUNGOL-treated cats (36/40) achieved at least one negative culture by the end of the study. Improvement was seen in inoculation site erythema and skin thickening by Day 7 and in crusts and scales by Day 14. By the end of the study, 98% of ITRAFUNGOL-treated cats had complete resolution of all clinical lesions, compared to 15% in the control group. Wood’s lamp cure (defined as no fluorescence at the base and mid-shaft of the hair) in the ITRAFUNGOL-treated group (39/40 or 97.5%) was higher compared to the control group (6/40 or 15%). Itraconazole MIGs indicative of susceptibility were obtained in M. canis isolates from the two cats unsuccessfully treated with ITRAFUNGOL.

Field Study
A masked, positive-controlled, multi-site field study was conducted in client-owned cats in Europe. In this study, 514 cats diagnosed with dermatophytosis were randomly administered itraconazole oral solution or an active control. Cats received a daily dose of either itraconazole oral solution for five alternating weeks plus a placebo tablet once daily for 5 consecutive weeks, or a placebo solution for three alternating weeks plus the active control once daily for 5 weeks. Success was evaluated on clinical cure, which was noted with a complete resolution of all clinical lesions. Four weeks after the end of treatment, 175 (83%) out of 207 cats treated with itraconazole oral solution were clinically cured.

Animal Safety:

Reproductive Safety
In a study of 16 pregnant queens administered itraconazole oral solution at 5 mg/kg bodyweight for a total of 21 days (7 days on alternate weeks) during gestation or lactation, there was a high frequency of fetal resorption (partial and total), abnormal fetuses, and abnormal maternal behaviors. Confounding factors, such as infectious disease (Chlamydia psittaci) in some cats made it difficult to establish a definitive relationship between administration of itraconazole and the abnormal findings. However, the results of this study reveal potential reproductive safety risks and do not support the safe use of ITRAFUNGOL in pregnant queens.

Storage conditions:

How supplied:
ITRAFUNGOL (itraconazole oral solution) is available in a glass bottle containing 52 mL of oral solution, closed with a child resistant screw cap and packaged in a cardboard box that includes a package insert and a graduated dosing syringe.

NADA 141-474, Approved by FDA.

Manufactured for Elanco US Inc.
Greenfield, IN 46140

Version Date: September 2016

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Pain Control for the Aging Horse

By Amanda Landis-Hanna, DVM

(continued from front cover)

is 25 years, so horses are considered geriatric once they reach age 18. It is important to consider that cold bloods (draft breeds) generally age more quickly and have a shorter lifespan overall.

OLDER AGE IS A DISEASE

Despite the notion that “old age is not a disease,” aging is a progressive physiologic disease that may be hastened by a number of factors, noted Dr. Bidwell, who is the owner and co-founder of East-West Equine Sports Medicine in Lexington, Kentucky. Concurrent disease, stress, chronic pain, malnutrition, lack of exercise, and the environment all contribute to the aging process and may increase the rate of deterioration.

The physiologic systems most likely to be impacted by the aging process include the cardiovascular, musculoskeletal, nervous, pulmonary, renal, and hepatic systems. As horses age, they lose both muscle mass and body water; these changes decrease the metabolic rate and affect the response to various drugs. In particular, older horses will have fewer circulating serum proteins, so drugs that are protein bound may have a higher circulating concentration.

A significant concern for the older horse is the risk for dementia. Opiates have been associated with signs of dementia in horses, so caution should be used with that class of drugs. Additionally, any drugs that cause vasoconstriction, such as atropine, may increase the dementia risk due to decreased blood flow to the brain.

Neuropathic pain is a malfunction of the nervous system whereby the nerve itself is the source of the pain instead of merely transmitting a pain signal. This type of pain may be seen in horses with chronic arthritis and chronic laminitis. Gabapentin (2.5 to 10 mg/kg PO q12h) may be used to treat neuropathic pain. The United States Equine Federation (USEF) has a 14-day withholding period for gabapentin.

PHARMACOLOGIC PAIN MANAGEMENT

Nonsteroidal anti-inflammatory drugs are the gold standard for treating pain in the geriatric horse, but it is important to monitor bloodwork and quality of life. Additional options for pain management include opioids, gabapentin, lidocaine, and herbal supplements. Dr. Bidwell has experience using aspirin 80 mg + omega-3 fatty acids, as well as flunixin, phenylbutazone, and firocoxib.

Multiple opiates may be used in the aging horse but, as noted earlier, it is important to monitor patients for dementia. Morphine is an inexpensive mu receptor that may be injected in many locations. Butorphanol may be given subcutaneously and has a duration of action of 2 to 5 hours; this method can be effective for abdominal pain. Dr. Bidwell often gives butorphanol with alpha-2 drugs to minimize excitation and enhance analgesia.

Buprenorphine is a partial mu agonist and a kappa agonist. Sustained-release buprenorphine is a compounded version of the drug that is given subcutaneously and lasts 2 hours. Methadone is a class II controlled substance available with multiple routes of administration. This mu receptor agonist is available as fast-dissolve tablets for oral administration and an injectable formula. Fentanyl is a short-acting pure mu agonist available in injectable, patch, and gel formulations.

When considering other pain control options, Dr. Bidwell recommends evaluating lidocaine, which can be used topically, transdermally, subcutaneously, intramuscularly, or intravenously. Lidoderm patches have 700 mg lidocaine in a 10×14-cm patch. About 3% (21 mg) of the patch is absorbed locally rather than systemically, and the patch may be cut to the shape of a wound. Analgesia will begin about 2 hours after placement and will wane after 11 hours. Clients may be taught to apply or exchange patches. Due to the high drug concentration, great care should be used to prevent accidental oral ingestion by children or dogs.

ALTERNATIVE PAIN CONTROL MEASURES

In addition to traditional analgesics, other compounds or medications may be used to support comfort in the aging horse. Dr. Bidwell recommends becoming familiar with various supplements, although she noted, “I am amazed by how often a new compound comes out.”

Anti-anxiety medications may be used to help ease discomfort. Many of these may be given as feed supplements. Despite having no analgesic properties of its own, acepromazine may be given to allow other medications to be more effective.

Sarapin is a P-blocker compound made from the Sarraceniaceae family (pitcher plant) that has local anesthetic and anti-inflammatory effects. The salts of the plant are placed in a sterile solution for intravenous, subcutaneous, intramuscular, or joint injections. In humans, this compound may be used for neuropathic pain; due to its plant origin, it is sometimes referred to as a “veggie block.”

A variety of herbal remedies are available as well. Dr. Bidwell recommends researching the source of each compound, as some may be less efficacious or may be from untrustworthy sources. Dr. Bidwell routinely uses Jing Tang Herbal Body Sore to treat chronic discomfort, but it is important to understand the Fédération Equestre Internationale (FEI) and USEF regulations related to herbal combination therapy.

Traumeel and Zeel are combinations of arnica, echinacea, and deadly nightshade given for their analgesic and anti-inflammatory properties. These compounds are legal for use within FEI and USEF regulations.

Resveratrol is a phenol compound designed to reduce gene expression of inflammatory enzymes. Equithrive is an equine variation of Resverasyan, a microencapsulated form of resveratrol.

Electroacupuncture will cause a release of opioid peptides, but may be given to allow other medications to be more effective.

CONCLUSION

It is always important to assess the goals and capabilities of the client when choosing a therapeutic protocol for managing pain. Appropriate setting of expectations will be rewarding for all who are caring for aging horses.

AMANDA LANDIS-HANNA, DVM

Dr. Landis-Hanna, a 2002 graduate of Auburn University, has practiced small animal, exotic, shelter, and relief medicine. She was a medical director at VCA for 7 years and served as director of veterinary medicine for Vyode. She is currently the senior manager of veterinary outreach for PetSmart Charities.
Chemotherapy-Induced Vomiting and Inappetence

A survey of veterinary cancer specialists reveals which chemotherapeutics oncologists commonly avoid and which drugs they use to address these common adverse effects in their patients.

By Laurie Anne Walden, DVM, ELS

In a poster presented at the 2017 American College of Veterinary Internal Medicine (ACVIM) Forum in National Harbor, Maryland, researchers from Iowa State University reported results of a survey of veterinary specialists’ perceptions of vomiting and inappetence caused by chemotherapy drugs. Respondents tended not to use the agents seen as most likely to cause significant vomiting. Maropitant was the drug most commonly prescribed to treat vomiting and inappetence in patients receiving chemotherapy.

Survey coauthor Chad M. Johannes, DVM, DACVIM (SAIM, Oncology), assistant professor of small animal internal medicine and oncology at Iowa State University, sat with American Veterinarian® staff to discuss the implications of the survey.

Investigating therapies that reduce the adverse effects of cancer treatment is important, he said, “because it’s those side effects that affect quality of life and ultimately clients’ willingness to pursue therapy.” The adverse effects of chemotherapy can be severe enough to stop treatment, he added.

The incidence of chemotherapy-induced vomiting and inappetence in dogs has not been reported, wrote the study authors. Unlike in human medicine, there is no standard protocol for their daily practice. Survey topics were as follows:

- Perceived incidence of acute and chronic vomiting after single administration of 20 chemotherapeutics
- Severity of vomiting caused by each drug (TABLE 1)
- Use of antiemetics for prevention and treatment of chemotherapy-induced vomiting
- Use of appetite stimulants in patients receiving chemotherapy

SURVEY RESULTS

Survey respondents perceived that single-agent chemotherapy drugs were well tolerated. They indicated that cisplatin, streptozocin, dacarbazine, paclitaxel, and epirubicin were most likely to cause significant vomiting when used as individual agents. These 5 drugs were also prescribed by the fewest survey respondents.

The antiemetics most likely to be used by respondents were maropitant, ondansetron, metoclopramide, and dolasetron. Survey respondents used antiemetics more often to prevent acute vomiting (day 1 of chemotherapy) than delayed vomiting (days 2–5 after chemotherapy) (TABLE 2).

SURVEY RESPONDENTS AND TOPICS

The investigators solicited survey responses through the ACVIM oncology and small animal internal medicine listservs. They received 85 completed surveys, including 71 from oncologists and 14 from internists. The majority of respondents (71%) reported that medical oncology accounted for at least 80% of their daily practice. Survey topics were as follows:

- Perceived incidence of acute and chronic vomiting after single administration of 20 chemotherapeutics
- Severity of vomiting caused by each drug (TABLE 1)

TABLE 1. Veterinary Cooperative Oncology Group – Common Terminology Criteria for Adverse Events (VCOG-CTCAE) Following Chemotherapy or Biological Antineoplastic Therapy in Dogs and Cats v1.0

<table>
<thead>
<tr>
<th>VCOG GRADE</th>
<th>CLINICAL DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&lt;3 episodes in 24 hours; medical intervention not indicated</td>
</tr>
<tr>
<td>2</td>
<td>3–10 episodes in 24 hours; &lt;5 episodes/day for &lt;48 hours; parenteral fluids (intravenous or subcutaneous) indicated &lt;48 hours; medications indicated</td>
</tr>
<tr>
<td>3</td>
<td>Multiple episodes &gt;48 hours; IV fluids or partial/total parenteral nutrition indicated &gt;48 hours</td>
</tr>
<tr>
<td>4</td>
<td>Life-threatening (eg, hemodynamic collapse)</td>
</tr>
<tr>
<td>5</td>
<td>Death</td>
</tr>
</tbody>
</table>

The drugs most commonly prescribed to stimulate appetite in patients receiving chemotherapy were maropitant, mirtazapine, and metoclopramide. The authors noted that maropitant was the drug most commonly used by respondents to treat both vomiting and inappetence.

IMPLICATIONS

Defining how veterinary oncologists and internists currently treat chemotherapy-induced vomiting and inappetence may help specialists develop guidelines for treating these adverse events, said Dr. Johannes. “The better that we can focus on improving quality of life, the better for our patients, the better for our clients, and the better for our outcomes.”

References available at AmericanVeterinarian.com.
Fear-Based Aggression in Dogs

Understanding when fear-based aggression is most likely to occur, plus how to identify and manage it.

By JoAnna Pendergrass, DVM

(continued from front cover)

If an owner comes in with an aggressive dog, it's important to remember that “aggressive behaviors are not pictures, they’re movies,” he advised. Rather than being static, the aggression has progressed over time.

RECOGNIZING FEAR IN DOGS

To diagnose fear-based aggression, it is important to evaluate the overall history, determine when the aggression occurs, and observe the dog's body postures during threatening situations.

Dr. Ciribassi cautioned against assuming that a fearful dog has a history of being abused.

In a threatening situation, a fearful dog initially will display defensive behaviors, which often go unrecognized because many pet owners are not familiar with canine body language: ears back, tail tucked, head down, piloerection, averted gaze, underbelly exposed, weight shifted backward, lips retracted, vertically and teeth exposed, and urinating, defecating, and expressing anal sacs.

If these postures do not ameliorate the situation, the dog will escalate its behavior and become overtly aggressive—often explosively—to manage the threat. “If a subtle technique, like looking away or yawning, doesn’t achieve the desired result,” Dr. Ciribassi said, “then the dog is going to be motivated to try something else.” Therefore, if aggressive behavior manages the threat effectively, the dog will learn to use it more efficiently and as a first resort. “If a dog learns that the use of aggressive behavior in perceived threatening situations is an effective strategy to manage those situations, then the use of aggressive behavior becomes reinforced.”

Dr. Ciribassi also described dominance-based aggression, given that many cases of fear-based aggression are misdiagnosed as dominance-based, leading to aversive-type treatment methods that actually worsen a dog's fear. “In my opinion,” he said, “most of those cases of aggression are fear-based, so if we use punishment-based techniques we tend to escalate the problem.”

Dominant behavior, characterized by confident body postures and ritualistic displays, usually begins at social maturity and is used to establish a hierarchy. Interestingly, dogs may progress from defensive to dominant body postures if they learn how to use aggression to successfully manage a situation; the defensive postures can return, however, in overwhelmingly threatening situations.

FEAR-INDUCING SITUATIONS

Fear-based aggression commonly occurs during leash walks. The leash can transmit the owner's anxiety and make it difficult for dogs to display typical aggressive behavior. Fearful dogs on a leash may display aggression as an unfamiliar person or dog is walking away.

Fear can also result from an owner trying to establish dominance over the dog, using strong physical or verbal punishment, or having inconsistent interactions with the dog. In turn, the dog may become fearful and resort to fear-based aggression (BOX).

MANAGING FEAR-BASED AGGRESSION

Addressing fear-based aggression in dogs requires a team approach, involving the owner, the veterinarian, and a professional animal behaviorist. The primary management options are removing triggers, redirecting aggressive behavior, and medical management.

Managing triggers may involve separating the dog from the trigger. For example, if strangers trigger fear-based aggression, keep the dog in a separate room when unfamiliar people visit. Another option is response substitution, in which the owner distract the dog and redirects inappropriate behavior to more appropriate responses that can be reinforced. Pet owners should avoid reinforcing aggressive behavior with positive attention; in other words, don’t tell the dog “it’s OK.”

Redirecting the behavior involves counter conditioning to train the dog to perform behaviors that are counter to the problem behavior. This can be done through operant or classical conditioning. In both scenarios, the dog is asked to perform behaviors it already knows, and these behaviors should be reinforced. A fearful dog should learn to seek its owner's direction during a threatening situation.

Medical management is indicated for fearful dogs that are overly reactive and do not follow direction or take rewards. This typically involves serotonin pathway reactivation to reduce amygdala-induced reactivity. Dr. Ciribassi recommended the selective serotonin reuptake inhibitors (SSRIs) fluoxetine, paroxetine, and sertraline. He also recommended clonidine and trazodone, both of which can be used situationally and in combination with an SSRI.

Dr. Ciribassi cautioned against managing fear-based aggression with amitriptyline because dogs can quickly build tolerance to it. In addition, benzodiazepines would not be a good medical management option because they can disinhibit fear, possibly encouraging a dog to display aggression. ■

BOX. Typical Fear-Inducing Situations That May Lead to Aggression

- An approaching stranger or unfamiliar dog while on a leash walk (the leash prevents escape and transmits owner anxiety; it also prevents typical dog–dog communication)
- A stranger entering the home or moving suddenly while in the home
- Reaching toward a dog’s head
- Young, mobile, active children (ie, unpredictability)
- Being punished

AmericanVeterinarian.com 21
Repair Surgery Among Latest Treatments for Mitral Valve Disease

We highlight exciting new and upcoming advances in the treatment of the most common heart disease in dogs, plus a pet owner’s account of her dog’s reparative surgery.

By Kim Campbell Thornton

Simon Swift, VetMB, DECVIM-CA, clinical associate professor of cardiology at the University of Florida, hopes to introduce the surgery to North America. He is heading up a 3-year plan to put together a surgical team to perform the procedure in the United States. Dr. Borgarelli is working on a technique in which a device is used to repair or replace the chordae tendineae, which hold the mitral valve in place but can stretch or rupture, worsening mitral regurgitation. The device would also be used to perform mitral annuloplasty to reduce the dimension of the valve’s orifice, decreasing regurgitation.

KIM CAMPBELL THORNTON

Kim Campbell Thornton has been writing about dogs and cats for 32 years. She is the award-winning author of more than 2 dozen books and hundreds of articles on pet care, health, and behavior.

The technique is not easy to master; other surgeons have tried to replicate it but with limited success.

Simon Swift, VetMB, DECVIM-CA, clinical associate professor of cardiology at the University of Florida, hopes to introduce the surgery to North America. He is heading up a 3-year plan to put together a surgical team to perform the procedure in the United States. Dr. Borgarelli is working on a technique in which a device is used to repair or replace the chordae tendineae, which hold the mitral valve in place but can stretch or rupture, worsening mitral regurgitation. The device would also be used to perform mitral annuloplasty to reduce the dimension of the valve’s orifice, decreasing regurgitation.

Sabine Bozon, DVM, and her husband, Jean-Hugues Bozon, DVM, who co-own Clinique Veterinaire Bozon in Versailles, France, lead the surgical team that performs the mitral valve repair in France, in partnership with Dr. Uechi. While the Bozons and Dr. Uechi would like the procedure to be more widely available, Dr. Bozon warns that the technique is not easy to master, noting that other veterinary surgeons have tried to replicate it but have met with limited success.

Following mitral valve surgery, Harper received stem cells, an experimental treatment that is thought to have an anti-inflammatory effect.
success. She credits Dr. Uechi’s success rate to years of practice and a surgical team that can recognize and react quickly to many complications.

Even if mitral valve repair surgery becomes available in the United States, Timothy Hodge, DVM, DACVIM (Cardiology), a cardiologist at the University of California Veterinary Medical Center in San Diego, does not foresee it becoming a mainstream procedure. “The procedure requires the most advanced equipment and a large, specially trained team,” he says.

The best candidates for mitral valve repair surgery are young to middle-aged dogs in otherwise good health. Dogs with certain health conditions, such as Cushing's disease or protein-losing enteropathy, are at greater risk for complications, as are dogs older than age 12 or 13. When surgery is successful, patients have an excellent prognosis. “Once dogs have their valve repaired, they don’t die of this disease. Generally speaking, they die of something else,” Dr. Swift says.

Despite the significant improvements it has made in dogs with degenerative MVD, there are drawbacks to the surgery that prevent its widespread implementation. These include its limited availability, high cost, and certain inherent risks with cardiopulmonary bypass, says Sarah Miller, DVM, DACVIM (Cardiology), who practices at Southern California Veterinary Specialty Hospital in Irvine.

**MEDICAL MANAGEMENT**

Not every owner can afford to have a dog’s mitral valve repaired surgically, and not every dog needs it. Medical management alone can add years to a dog’s life. “Some dogs are very good on medical treatment until death,” Dr. Bozon says. “It depends on the gene involved and how fast the disease is progressing.”

The medications used have not changed substantially over the past 10 years, but there are updates in when they are used. One example is pimobendan, which has been shown to delay death in dogs with degenerative MVD once they are in heart failure, Dr. Swift says, adding that the results of a study published in 2016 in the *Journal of Veterinary Internal Medicine* suggest that starting the drug in the preclinical stages once there is heart enlargement will delay the onset of heart failure itself.2

Even with medical treatment, dogs generally live only 9 to 12 months after the onset of heart failure, so delaying it can add time to a dog’s life. “If we can delay heart failure by significant periods of time, that’s definitely worth doing,” Dr. Swift says. “Some people do have concerns about whether pimobendan is harmful at that point, but I have yet to see any data to support that.”

For general practitioners, the important thing to know about pimobendan is when to prescribe it. It should not be given before the heart becomes enlarged. “Patients qualifying for early pimobendan use based on the EPIC study generally speaking must have at least a [grade] 3/6 left apical systolic murmur and moderate left heart enlargement diagnosed via thoracic radiographs and on echocardiogram,” Dr. Miller says. “The study clearly demonstrated a delay in the onset of congestive heart failure; however, it is too soon to say if this benefit has been reproduced clinically.”

Diuretics are prescribed for any dog with signs of fluid in the lungs or abdomen. The standard diuretic is furosemide, which rids the body of excess fluid. However, the disease can reach a stage at which furosemide is no longer effective, reducing the diameter of the mitral annulus. During the 90-day recovery period, the dog’s activity level is limited: no jumping, running, or excessive excitement.

After Harper’s left atrium was closed, her heart restarted on its own, although some dogs need assistance. She was released after a week of hospitalization, which included 2 stem cell treatments. Her heart had returned to its normal size, and mitral regurgitation had decreased by more than 90%. We flew home 3 days later.

Harper no longer needs her presurgery medications, but she took clopidogrel (Plavix), sildenafil, and fragmin during the first month after surgery. At Harper’s 1-month checkup, Dr. Miller discovered a small pulmonary blood clot and Harper had to begin heparin injections 3 times a day, but Dr. Bozon expects the clot to dissolve in 2 to 4 weeks.

**A Good Outcome**

A common question about the surgery is how long dogs will live afterward. Barring other illnesses or injuries, a dog should live a normal lifespan for its breed. Dogs are known to have lived 7 to 9 more years after the mitral valve repair surgery, Dr. Bozon says. The potential lifespan for a Cavalier is 13 to 17 years, so we hope to enjoy Harper’s company for some time to come.

—KCT

(continued on page 24)
even in large doses. In those cases, Dr. Swift says, there are two options. “You can add in a thiazide diuretic, which often helps because it blocks different bits of the kidney, or you can switch the dog from furosemide to a diuretic called torsemide, which is more potent,” she says. “We’ve had a lot of success with dogs being fairly end stage not responding to oral furosemide and we switch them to torsemide and they’ve done very well.”

It used to be thought that angiotensin-converting enzyme inhibitors, such as enalapril and benazepril, might delay the onset of congestive heart failure in dogs that were asymptomatic, but there is no evidence to support that, says Dr. Swift.

The fourth drug that can benefit dogs with degenerative MVD is spironolactone, a mild diuretic that is more properly thought of as an anti-aldosterone agent. Aldosterone is a hormone that gets upregulated in heart failure. Because it is toxic to myocardial cells, causing fibrosis and cell death, it can accelerate disease progression, Dr. Swift says.

**DIAGNOSTIC AND TREATMENT CHALLENGES**

One of the challenges of MVD is getting a correct diagnosis. Not every veterinarian or client has access to a board-certified cardiologist. “Echocardiography is the best noninvasive way to diagnose heart disease in dogs,” Dr. Hodge says. “Cardiologists receive advanced training specifically to perform and interpret echocardiography.”

The same issue makes treating the disease a challenge. Dr. Hodge says a study published in 2016 found that dogs cared for by a primary care veterinarian and a board-certified cardiologist working together had longer survival times than dogs that did not have a cardiologist involved in their treatment.1

Another problem is the common but mistaken assumption that a dog with a murmur that coughs must be in heart failure. “That is absolutely not true,” Dr. Swift says. “The main reason dogs cough is because either they have primary airway disease or they have a big heart that’s compressing their airways. So, they will cough way before they have heart failure. Starting those patients on heart failure medication may be inappropriate. We see a lot of dogs that are put on high doses of diuretics for coughing, and actually they’re not coughing because they’ve got heart failure. Of course, they don’t get better, and what happens is the dose gets escalated. They can reach really high doses of diuretics before they get referred in [to a cardiologist].”

Even when they are necessary, high doses of diuretics can be frustrating for owners. Their dogs start having housetraining accidents or leaking urine in their sleep. “The most common mistake I see is when dogs are being managed successfully for congestive heart failure and either the owner or the referring veterinarian attempts to taper or stop the diuretic therapy,” Dr. Miller says. “These dogs often present in respiratory distress on an emergency basis due to recurrent congestive heart failure, requiring more aggressive therapy for their disease and additional hospitalization cost and stress for the patient and owner.”

**RESEARCH UNDER WAY**

Researchers are exploring several possible treatments for degenerative MVD as well as continuing to seek the cause. At Cornell University, Vicky Yang, DVM, PhD, DACVIM (Cardiology), is evaluating the data from a small pilot study of the effects of stem cells and hopes to have results later this year. “We thought if mesenchymal stem cells are antifibrotic and anti-inflammatory, they could have a beneficial effect in controlling fibrosis in these heart valves,” she says.

A genetic therapy for Cavalier King Charles spaniels with the disease is the subject of a partnership between Harvard Medical School and Tufts University. However, the researchers preferred not to discuss their work until the trial is complete later this year.

Some veterinary surgeons, such as Christopher Orton, DVM, PhD, DACVS, at Colorado State University, are seeking a noninvasive method of valve replacement or repair, but the small size of many of the dogs that develop degenerative MVD—Cavalier King Charles spaniels, Chihuahuas, toy and miniature poodles, and Dachshunds are among the breeds in which it’s commonly seen—limits what can be done noninvasively to treat the disease.

“Catheter-based interventions will likely be the future treatment of choice, but the equipment is too large to be used currently in our small patients,” says Dr. Miller.

Dr. Borgarelli is also studying valve morphology in Cavaliers. The Cavalier mitral valve has smaller, flatter leaflets than those of other dogs. “It looks like maybe the valves of these dogs have some disadvantages compared with valves from other breeds,” he says. “That may play a role in the development of disease. We are planning to do a longitudinal study that will look at the morphology of the valve and its relationship to age at onset of disease. I think that’s something that in the future could be important for screening.”

But a cure or treatment that is affordable and can extend life for many years is probably still far in the future. “Current research aims to evaluate why cardiac diseases are so prevalent in certain types of dogs or certain breeds,” says Dr. Hodge. “The answers may lie in genetic mutations, which may develop into targets for gene therapy. But as of right now, I do not know of anyone currently having success with these possible treatments.”

**References available on AmericanVeterinarian.com.**
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always read, understand and follow label and use directions.
The Benefits of Chiropractic Care

These treatments are used to address a wide variety of health issues in animals, and more veterinarians are choosing them.

By Don Vaughan

(continued from front cover)

and determined that she would benefit from having a brace on it. “Regina was fitted for the brace during that examination, and Dr. Peyton also recommended chiropractic adjustment after observing the tension and misalignment in Regina’s back, shoulders, and neck,” reports Alicia Pell, Farm Sanctuary’s southern California shelter manager.

The results have been impressive. Prior to her first adjustment, Regina exhibited decreased mobility and activity, Pell noted, but immediately afterward, her activity level improved noticeably. “She moved around much more, and her movement appeared less stiff and painful,” Pell observed. “The differences in activity and mobility were fairly substantial.”

CHIROPRACTIC: A BRIEF HISTORY

The first chiropractic adjustment was performed in 1895 by Daniel David Palmer of Davenport, Iowa. Two years later, Palmer established the world’s first school for chiropractic. Interestingly, animals were among Palmer’s first “patients,” as he worked to prove that the benefits of chiropractic manipulation were more than just a placebo effect. As chiropractic gained acceptance among human health care providers, so, too, did veterinarians come to realize its value. Today, 40 states provide regulatory guidelines for the practice of chiropractic care and related treatments on animals.

“The overall goal of chiropractic care is improved mobility, pain relief, and the general health of the patient,” says Dr. Peyton. “Best of all, it’s appropriate for all species.”

Dr. Peyton received her chiropractic training in 2016 from Options for Animals College of Animal Chiropractic in Wells-ville, Kansas, and was certified through the International Veterinary Chiropractic Association, 1 of 2 bodies in the United States that certify veterinarians and human chiropractors to work on animals. “I didn’t quite understand the role of chiropractic in helping our patients,” Dr. Peyton says, “but since I took the certification class and have been actively incorporating chiropractic into my patient care, I have really become a proponent.”

Despite growing advocacy, many veterinarians remain wary of chiropractic care and are reluctant to incorporate it into their practices.

CHIROPRACTIC: A BRIEF HISTORY

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BENEFITS BEYOND BACK PAIN

Dr. Peyton also has introduced chiropractic to her students, many of whom, she says, come to class with preconceived ideas about what chiropractic care is and its role in veterinary medicine. “When they watch me treat a patient, they realize just how precise this modality is as I adjust each joint individually,” she says. “They also see how it benefits the patients. My goal is to open their minds to the idea that there are other modalities they can incorporate to help their patients.”

As in human medicine, veterinary chiropractic is used to treat a wide variety of health issues, reports Patty Glover,
DVM, owner of Naturally Balanced Veterinary Services in Pulaski, Wisconsin, a practice that specializes in chiropractic, acupuncture, and the use of Chinese herbs. Musculoskeletal discomfort, she says, is one of the primary presentations in her patients. “In small animals, we see a lot of intervertebral disk disease,” Dr. Glover notes. “We also see a lot of arthritis patients and performance animals, such as dogs and horses, that are stiff or not competing well.”

Darby, a 12-year-old Boston terrier owned by Kelli Daniel sen of Oakland, California, is a good example of this type of chiropractic patient. He receives regular adjustments from Dr. Peyton for arthritis/spondylosis due to a defect in the structure of his spine and has benefited greatly, Danielsen says. “Darby had a good amount of atrophy in his hind legs and less coordination before he started seeing Dr. Peyton,” she reports. “He is now more active and coordinated than a few years ago and more confident in his movements. The treatments have definitely improved his quality of life.”

Chiropractic also can have a big impact on health issues related to the nervous system, notes Dr. Glover, who has been providing chiropractic services for 13 years. “Many of my patients receive chiropractic adjustments for issues outside the traditional complaints,” she says. “For example, I see a lot of urine dribblers. By helping the nerves to function well from the lower back through the sacrum, their bladders function more normally so they stop dribbling urine. Other nontraditional issues I’ve addressed through chiropractic include anxiety and seizures.”

According to Dr. Peyton, the typical chiropractic session begins with a thorough patient history that explores specific health issues, the animal’s home environment, and more. A general physical exam is next. “When I enter the room, I’m talking to the owner but I’m also looking at every aspect of movement from the animal,” Dr. Peyton explains. “How does it walk around? Is 1 leg weaker than the other? Does it have trouble sitting or lying down? During the physical, we may also do an orthopedic and neurologic exam.”

Following the physical exam, Dr. Peyton conducts a chiropractic examination. “Starting at the head, I go through each joint in the vertebral column, the facet joints, and move them—what we call joint motion palpation,” she says. “If I assess that an area is not moving well, I will define it as a vertebral subluxation and do an adjustment, which is a high-velocity, low-amplitude force to get the joint to move better and stimulate the neurologic receptors on the joint capsule. If an animal has a chronic disease, this will probably be a long-term part of its maintenance care.”

GROWING INTEREST AMONG VETERINARIANS

As the benefits of chiropractic care have become better understood, interest in the technique has grown among veterinarians. Leslie Means, executive director of the Oklahoma-based American Veterinary Chiropractic Association (AVCA), reports that since 1989, the AVCA’s certifying body, the Animal Chiropractic Certification Commission, has certified 1235 doctors of veterinary medicine and doctors of chiropractic to work on animals. Doctors must recertify every 3 years, Means notes.

“We’re seeing a much stronger interest in chiropractic,” confirms Heidi Bockhold, DC, owner of Options for Animals College of Animal Chiropractic. “Traditionally, the classes that we teach have seen an even mix between veterinarians and doctors of chiropractic. Now, it is consistently more like 70% to 75% veterinarians.”

Dr. Bockhold credits this jump to the growing number of animal owners who appreciate chiropractic and want it for their pets as well as a greater overall understanding of integrative medicine within the veterinary community.

But despite growing advocacy, many veterinarians remain wary of chiropractic and are reluctant to incorporate it into their practices. “I believe the biggest misconception among veterinarians is what chiropractic really is,” says Dr. Glover. “The general concept is that your back is out and a chiropractor will put it back in, but the reality is that chiropractors work on a much more subtle level. So, when veterinarians start to understand that I’m addressing issues related to an animal’s range of motion, their interest piques.”

Indeed, despite the reluctance from some practitioners, most advocates of integrative medicine believe chiropractic has a bright future in veterinary medicine. “It’s getting stronger and stronger, and I think it will become even more mainstream,” says Dr. Bockhold. “It’s too powerful to ignore. It’s a young profession that is growing very rapidly, but it needs to be a collaborative endeavor between veterinarians and chiropractors.”

BOX. Integrative Medicine: A Complementary Approach

Chiropractic is just one aspect of integrative medicine that is available to veterinarians. Others include acupuncture, massage, Chinese herbs, homeopathy, and aromatherapy, all of which may be used as complements to chiropractic treatment, says Jamie Peyton, DVM, DACVECC, from the University of California, Davis, Veterinary Medical Teaching Hospital.

“We use traditional medicine, but then we incorporate these other modalities to help minimize the side effects of certain drugs or to increase pain control in our patients,” Dr. Peyton explains. “They provide more tools for the doctor’s toolbox.”

Patty Glover, DVM, owner of Naturally Balanced Veterinary Services in Pulaski, Wisconsin, practiced traditional medicine in an equine practice until she became certified in chiropractic by the International Veterinary Chiropractic Association. In 2011, she quit traditional practice to offer integrative medicine exclusively, specifically chiropractic and acupuncture, and today sees all species. “There are some things that traditional medicine treats well, and quite honestly, there are others that it doesn’t,” Dr. Glover notes. “I believe chiropractic and other forms of integrative medicine are very important for our animal patients for many reasons, but especially because they are needed to fill those gaps in health care.”

Many veterinarians have started incorporating integrative medicine into their practices because clients request it, Dr. Peyton adds. A change in culture will be required before all practitioners are on board. “There is a whole subset of practitioners who have yet to embrace integrative medicine, partially because they are unaware of the science around it,” she says. “We need to get the word out about how these modalities work and how they benefit our patients.”

One subgroup that benefits greatly from integrative medicine is oncology patients. “Integrative approaches, such as chiropractic and acupuncture, can help relieve the pain of treatment while also boosting the immune system,” Dr. Peyton said. “That is vital for recovery.”
Can Sleep Improve Memory in Dogs?

Hungarian researchers studied whether sleep has the same memory consolidation effect in dogs as it does in humans.

By JoAnna Pendergrass, DVM

We’ve all heard the familiar advice about getting a good night’s sleep before a test. Such advice is rooted in the theory that sleep functions as a mode of memory consolidation, which is the conversion of short-term memory into long-term memory. According to 1 study, when we sleep, our brains refresh memory circuits—an activity that is incompatible with the processing of sensory information that occurs while we’re awake.

Could this same memory consolidation take place in dogs when they sleep? The results of a study conducted by a team of researchers in Hungary recently revealed a connection between sleep and learning in dogs, providing novel evidence of sleep-dependent memory consolidation in man’s best friend.

To date, most studies evaluating the link between sleep and memory consolidation have been performed in humans and laboratory rodents. Sleep studies in dogs have focused primarily on brain activity with neurologic conditions such as epilepsy. According to the current study’s researchers, canine studies on sleep function could provide useful insight into the function of human sleep, given dogs’ long domestication history and humanlike social skills.

SLEEP CHARACTERISTICS

For dogs and other mammals, the sleep cycle consists of 3 main phases: nonrapid eye movement (non-REM) sleep, REM sleep, and wakefulness. Electroencephalogram (EEG) studies have demonstrated the cyclic brain wave activity throughout the sleep cycle (FIGURE):

- Beta waves: alert wakefulness
- Alpha waves: drowsy wakefulness
- Theta waves: REM sleep
- Delta waves: non-REM sleep

For the current study, the research team conducted a 2-part learning experiment to evaluate sleep and memory consolidation in dogs.

STUDY DETAILS

Part 1: The Effect of Learning on Sleep Physiology

The researchers first looked at how learning an unfamiliar verbal command affects brain wave activity. Fifteen adult pet dogs were selected based on their ability to follow verbal “sit” and “lie down” commands and to understand the hand signals for each command. Each dog participated in command learning (CL) and nonlearning (NL) scenarios in the afternoons on different days.

For the CL scenario, dogs first had a teaching session during which they learned unfamiliar English verbal commands for “sit” and “lie down.” Next, they had a baseline testing session of the English commands. Immediately following that
session, the dogs underwent 3-hour noninvasive polysomnography and were then retested with the English commands after awakening.

For the NL scenario, teaching and baseline sessions consisted only of familiar Hungarian commands for “sit” and “lie down,” immediately followed by 3-hour polysomnography. Dogs performed the same number of “sit” and “lie down” actions and received the same amount of food reinforcement in both scenarios; the only difference between the scenarios was the learning of new information or the lack thereof. Dogs were not retested in this scenario.

From the polysomnography recordings, researchers collected sleep structure data, including sleep duration and non-REM and REM durations. EEG spectral analysis was performed to evaluate the relative contribution of each wave frequency (beta, alpha, theta, delta) to the overall brain wave pattern. For only the CL scenario, behavioral data were collected to compare performance between the baseline and retest sessions and to evaluate the relationship between performance and brain activity.

Results
Contrary to the researchers’ expectations, but similar to findings in some human sleep studies, learning had no influence on the dogs’ sleep structure. EEG spectral analysis indicated a few notable changes in postlearning brain wave activity during REM and non-REM sleep. In REM sleep, theta activity significantly increased; in non-REM sleep, delta activity significantly increased and alpha activity significantly decreased. Within non-REM and REM sleep, slow-wave activity changes were inversely related to fast-wave activity changes. This finding, coupled with the decreased alpha activity in non-REM sleep, may have indicated deeper sleep after learning, the researchers noted.

In the CL scenario, performance significantly improved from baseline to retest, suggesting a positive effect of sleep on learning. Decreased delta activity and increased beta activity during REM sleep were significantly correlated with higher performance, whereas wave activity during non-REM sleep and theta and alpha activity during REM sleep did not correlate with performance.

Anna Kis, PhD, the study’s lead researcher, said via email that part 1 results indicate that the “individual sleep EEG spectrum is related to learning performance upon awakening, suggesting that differences in sleep pattern and brain activity during sleep have an effect on postsleep behavior.”

Part 2: The Effect of Sleep and Awake Activity on Learning
The researchers then evaluated how various postlearning activities affect learning. Fifty-three adult pet dogs underwent a similar CL scenario as in part 1. After that, instead of undergoing polysomnography, they participated in 1 of 4 activities during a 1-hour retention interval (RI):

- Playing with a Kong toy
- Learning a new command
- Sleeping in their owner’s car
- Leash walking around the university campus

Researchers did not include a “resting” awake RI activity because keeping a dog awake while resting could stress the animal, which would not only raise animal welfare concerns but also negatively affect memory. After the RI, dogs were retested with the English commands and had an obedience session with the Hungarian commands. One week later, dogs were tested again with the English commands to evaluate their long-term memory. The percentage of correct actions was calculated for all sessions (baseline, retest, obedience, long-term). Researchers compared performances among all sessions and used regression analysis to determine relationships between performance, test session (baseline, retest, long-term), and RI condition.

Results
Overall, performance was significantly related to test session, “suggesting that differential learning patterns emerged as a consequence of the various activities following the initial learning task,” the researchers wrote. Interestingly, performance did not significantly improve between baseline and retest for the sleep condition; this was likely due to the short RI duration. However, performance significantly improved at the long-term test session for the sleep, walk, and play conditions, suggesting that at-home night sleep after learning improves memory consolidation under certain conditions.

Performance remained relatively unchanged between test sessions for the learning condition, indicating that learning a new command can interfere with memory consolidation of the original command. For the play condition, performance significantly decreased between baseline and retest, potentially due to the emotional arousal of playtime.

MORE RESEARCH AND REAL-WORLD APPLICATIONS
According to the researchers, this study’s novel findings open the door for future research and real-world application of the link between sleep and learning in dogs. In the research realm, studies could examine whether age-related changes in sleeping, brain activity, and memory function influence memory consolidation in senior dogs. In addition, given the marked performance improvement following the 3-hour polysomnography—but not the 1-hour sleep condition—further evaluation is needed to determine the ideal amount of sleep required for adequate memory consolidation.

The effects of social interactions and environment on sleep patterns in dogs are other promising research areas. Dr. Kis mentioned her team’s ongoing research on the effects of positive and negative social interactions on sleep structure in dogs. Regarding an environmental effect, Dr. Kis and her team, in a limited number of observations, have also identified pattern differences in dogs sleeping in a laboratory setting versus in their home environments.

In the real world, understanding the relationship between sleep and learning is applicable to dog training. Allowing time for memory consolidation would help a dog master 1 task before learning another. ■
CHEWABLES

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

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

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

<table>
<thead>
<tr>
<th>Dog Weight</th>
<th>Chewables Per Month</th>
<th>Ivermectin Content</th>
<th>Pyrantel Content</th>
<th>Color Coding on Foil Backing and Carton</th>
</tr>
</thead>
<tbody>
<tr>
<td>Up to 25 lb</td>
<td>1</td>
<td>68 mcg</td>
<td>57 mg</td>
<td>Blue</td>
</tr>
<tr>
<td>26 to 50 lb</td>
<td>1</td>
<td>136 mcg</td>
<td>114 mg</td>
<td>Green</td>
</tr>
<tr>
<td>51 to 105 lb</td>
<td>1</td>
<td>272 mcg</td>
<td>227 mg</td>
<td>Brown</td>
</tr>
</tbody>
</table>

HEARTGARD® Plus is recommended for dogs 6 weeks of age and older. For dogs over 100 lb, use the appropriate combination of these chewables.

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

Care should be taken that the dog consumes the complete dose, and treated animals should be observed for a few minutes after administration to ensure that part of the dose is not lost or rejected. If it is suspected that any of the dose has been lost, redosing is recommended.

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

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

If the interval between doses exceeds a month (30 days), the efficacy of ivermectin can be reduced. Therefore, for optimal performance, the chewable must be given once a month on or about the same day of the month. If treatment is delayed, whether by a few days or many, immediate treatment with HEARTGARD Plus and resumption of the recommended dosing regimen will minimize the opportunity for the development of adult heartworms.

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

EFFICACY: HEARTGARD Plus Chewables, given orally using the recommended dose and regimen, are effective against the tissue larval stage of D. immitis for a month (30 days) after infection and, as a result, prevent the development of the adult heartworm.

SAFETY: HEARTGARD Plus Chewables are also effective against canine ascarids (T. canis, T. leonina) and hookworms (A. caninum, U. stenocephala, A. braziliense).

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

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

While some microfilariae may be killed by the ivermectin in HEARTGARD Plus at the recommended dose level, HEARTGARD Plus is not effective for microfilaria clearance. A mild hypersensitivity-type reaction, presumably due to dead or dying microfilariae and particularly involving a transient diarrhea, has been observed in clinical trials with Ivermectin Plus after treatment of some dogs that have circulating microfilariae.

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

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

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

ADVERSE REACTIONS: In clinical field trials with HEARTGARD Plus, vomiting or diarrhea within 24 hours of dosing was rarely observed (1.1% of administered doses). The following adverse reactions have been reported following the use of HEARTGARD: Depression/lethargy, vomiting, anorexia, diarrhea, mydriasis, ataxia, staggering, convulsions and hypersalivation.

SAFETY: HEARTGARD Plus has been shown to be bioequivalent to HEARTGARD, with respect to the bioavailability of ivermectin. The dose regimens of HEARTGARD Plus and HEARTGARD are the same with regard to ivermectin (8 mcg/kg). Studies with ivermectin indicate that certain dogs of the Collie breed are more sensitive to the effects of ivermectin administered at elevated dose levels (more than 16 times the target use level) than dogs of other breeds. At elevated doses, sensitive dogs showed adverse reactions which included mydriasis, depression, ataxia, tremors, drooling, paresis, recumbency, excitability, stupor, coma and death. HEARTGARD demonstrated no signs of toxicity at 10 times the recommended dose (80 mcg/kg) in sensitive Collies. Results of these trials and bioequivalency studies, support the safety of HEARTGARD products in dogs, including Collies, when used as recommended.

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

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

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

For customer service, please contact Merial at 1-887-637-4251.

Eliminating Canine Rabies From the Western Hemisphere

Much progress has been made in eradicating this deadly disease, but roadblocks remain, experts say.

By Nicola M. Parry, BVSc, MRCVS, MSc, DACVP, ELS

In a review article published last month, Andres Velasco-Villa, PhD, of the Centers for Disease Control and Prevention, and colleagues from around the world highlighted major milestones critical to eliminating dog-transmitted rabies in people and outlined impediments to achieving this goal.1

“We tried to present the information in a way that is accessible and raises awareness among key players in government, policy makers, and other stakeholders, so that they can make information-based investments to eliminate the dog-maintained rabies viruses, and to prevent rabies virus re-introductions from other natural sources, which requires sustained rabies herd immunity in dog populations,” Dr. Velasco-Villa said in an interview with American Veterinarian®.

BACKGROUND

Rabies is caused by viruses in the genus Lyssavirus of the family Rhabdoviridae. Rabies is the prototype species of the genus and causes disease in nearly all terrestrial mammals. The virus is transmitted from animals to people through bites or scratches, typically when saliva from the infected animal comes into contact with human mucosa or fresh skin wounds.
Rabies virus has a broad host range. Throughout its evolutionary history, the virus has established itself in a wide variety of species of bats and terrestrial carnivores, allowing it to circulate in independent maintenance cycles. "This host plasticity alone makes rabies eradication largely unfeasible," Dr. Velasco-Villa said. However, he added that the mode of transmission of rabies virus makes it highly unlikely that rabies could become pandemic in humans or susceptible mammals, particularly not in the same way that influenza and other airborne RNA virus pandemics arise.

Most cases of rabies in humans are caused by dog bites. However, this deadly disease can be prevented in both dogs and humans by vaccination. Indeed, large-scale vaccination of dogs against rabies has reduced the incidence of the disease dramatically in people in the Western Hemisphere over the past decade.

**THE IMPORTANCE OF HERD IMMUNITY**

According to the study authors, although eradicating dog-maintained rabies is an attainable goal, it requires permanent elimination of both dog-maintained and dog-derived rabies virus variants. Rabies herd immunity should be maintained above 70% in dog populations to avoid re-introducing the disease from other natural sources such as bats and wild animals, they stressed, and reaching this level could be challenging because of the high reproductive rate of free-roaming dog populations. "Ideally, sustained elimination of rabies from dogs will be feasible only if free-roaming dog populations are controlled," Dr. Velasco-Villa noted. Thus, programs focusing on complete elimination of this disease in dogs must consider also using humane methods of controlling these canine populations, he added.

**EFFORTS IN LATIN AMERICA**

The authors emphasized that, in Latin America, political recognition of canine rabies as a human public health problem was a turning point in the move toward sustainable rabies control and prevention programs. Today, the ministries of health handle all these activities, which previously were coordinated and funded by the ministries of agriculture in most Latin American countries. "The new initiative guaranteed sustained budgets for all activities related to rabies control and prevention in dogs, such as mass vaccination, creation and maintenance of a diagnostic infrastructure, construction of anti-rabies centers, support for dog population-control activities, and educational outreach," the authors wrote.

In addition to culling, surgical spaying and neutering have been used during mass vaccination campaigns in Latin America. Hormone-based vaccine-induced contraception also has shown promise in these areas. In this strategy, a contraceptive hormone component is incorporated into new-generation, single-dose rabies vaccines. "Single-dose vaccines comprise a highly attenuated (completely avirulent) replication-competent rabies virus, which has been genetically modified to become more immunogenic and carry a contraceptive component," Dr. Velasco-Villa said.

These types of vaccines will both reduce the number of doses needed to produce immunity and prevent the need to use surgical or chemical population-control measures. According to Dr. Velasco-Villa, if an oral formulation can be developed, the administration and distribution costs will decrease. Furthermore, this type of approach will make vaccination and dog population control a more affordable and humane alternative for resource-limited countries, where free-roaming dog populations are largely responsible for the chronicity of the problem," he said.

Indeed, these intense efforts to eliminate dog-maintained rabies virus variants in Latin America have dramatically reduced the human rabies burden in these countries. From 2005 to 2015, a 98% reduction in the number of rabies cases in dogs contributed to a 96% reduction in the number of rabies cases in people—from 285 cases in people in 1970 to just 3 in 2015.

**CHALLENGES TO ELIMINATING RABIES**

Some of the most significant barriers that hinder complete elimination of canine rabies include “limitation of monetary resources, public health prioritization, uncontrolled free-roaming dog populations, and cultural backlash,” according to Dr. Velasco-Villa. He stressed, however, that educational outreach regarding approaches that encourage more humane treatment of dogs could also help shift negative cultural behaviors that contribute to growing numbers of stray dogs throughout the world.

The authors emphasized that the significant decrease in the incidence of dog-maintained rabies in the Western Hemisphere, along with the nearly zero number of cases in people, could create a false sense of security among public health officials and governments. This could result in canine rabies no longer being considered a public health problem, leading to budget cuts or even elimination of strategic national control programs.

However, the authors stressed, there is a constant risk that epizootics could recur wherever “hot spots” of dog-maintained rabies and large populations of free-roaming dogs exist. In such instances, herd immunity decreases and dog-derived rabies virus variants continue to circulate near naïve dog populations, they said.

“The complete elimination of canine rabies, especially in ‘hot spots,’ requires permanent funding, with governments and people committed to bringing resources and elimination activities to those remote localities where the problem persists,” the authors concluded.

Reference available on AmericanVeterinarian.com.
Jon Geller, DVM, attended a veterinary conference in Nashville, Tennessee, a few years ago. Although he was there to gain information to support his high-tech emergency hospital in Fort Collins, Colorado, Dr. Geller gained a good deal more than that.

While taking a walk over a bridge during a break from the conference, Dr. Geller's eyes met those of a homeless man with a dog. The two connected ever so briefly, and as Dr. Geller continued his walk, he formulated a plan.

"I realized I wanted to help a fairly large subset of people who had no money whatsoever, who are totally left out of our veterinary efforts," said Dr. Geller. Of course, at his emergency hospital he had clients who loved their pets and wanted to provide treatment but couldn't afford it. There were programs available to help some of those clients, but the people he had in mind were different. He wanted to help those in the most down-and-out stratum of society, those who typically don't show up at an emergency facility. Today, Dr. Geller and his Street Dog Coalition provide free veterinary care to homeless people's pets throughout the country.

GETTING STARTED

Dr. Geller's desire—to provide veterinary services to homeless and indigent pet owners at no charge—came to him naturally. His mother, who had been involved heavily in animal rescue work, had recently passed away. On the day when his eyes met those of the homeless man, he had been thinking about his mother's selflessness.

To continue his mother's legacy, Dr. Geller used the money she left him to start a nonprofit that could really make a difference. “The plan resonated with me and I knew I would embark on this venture to care for these people, where money was totally left out of the equation," he said.

Thus, he founded the Street Dog Coalition, an all-volunteer organization whose mission is to provide free medical care and other services to pets of the homeless. In the group's first Street Dog Coalition Clinic in May 2015 in Fort Collins, a team of 5 veterinarians, 3 veterinary students, 4 veterinary technicians, and others provided free veterinary care for 30 dogs and cats. The care provided included vaccinations, heartworm testing and prevention, treatment of minor wounds and infections, pain management, and other services.

Dr. Geller found similarities between his day job and his nonprofit work.

"Working with limited resources was a challenge to medical skills as well," he said. "What you can learn from history and exam and how much you can do in a field situation uses skills that are complementary to emergency practice."
EXPANDING EFFORTS
Dr. Geller’s plan expanded to help others set up similar clinics. Today, the Street Dog Coalition has satellite operations in Wilkes-Barre, Pennsylvania; Boston, Massachusetts; and Tampa Bay/Sarasota, Florida. There are many advantages to teaming up with Dr. Geller and Street Dog (BOX).

This past spring, Dr. Geller arranged a Street Dog Coalition Clinic in Las Vegas associated with the Western Veterinary Conference (WVC). Both veterinarian and technician attendees volunteered their time.

These events don’t always go as planned. According to Dr. Geller, at the time of the clinic, there had been serial killings of homeless men sleeping on Las Vegas streets, so police and city officials showed up at the event. Homeless advocates later confirmed that the presence of authorities deterred many of the homeless pet owners in the area, because they feared legal retribution, deportation, or loss of their pet.

In addition, occasionally a pet shows up at these street clinics in urgent need of services that can only be provided at a veterinary hospital. Sometimes referrals can be negotiated, but usually euthanasia rather than treatment is the outcome because of the costs involved and the challenges of follow-up care.

I met Dr. Geller at the WVC clinic. A man of action, he plans to have Street Dog Coalition Clinics associated with many other conferences soon. If you have an opportunity to participate, jump at the chance. It was an over-the-top rewarding experience for me. The look on the face of a downtrodden person when you help his or her pet is priceless. My heart felt full on the bus ride back to the conference.

When I spoke with Dr. Geller recently, he encouraged me to get started in my own hometown. “Find a homeless day center or shelter and take 3 appointments once a week. That’s what I did,” he said.

Dr. Geller said, “There are really 3 components to my work with the homeless. First, I’m giving up 1 to 2 hours a week at the day shelter in my local community. It is not expensive for me to do that—any veterinarian could. Just think of how many practicing veterinarians there are in the United States. If each gave up just a few hours a month, there would be enough service hours to take care of a large number of pets for those without the financial resources to pay for veterinary care. Second is the Street Dog Coalition Clinics we do regionally, like those in Boston or Pennsylvania, a few times a year. Third is the convention work like WVC or other national events, like the work we’ll be doing with veterans in November in Washington, DC.”

COMING FULL CIRCLE
This fall, Dr. Geller will be teaming up with local veterinarians leading a Street Dog Coalition Clinic at the International Veterinary Emergency and Critical Care Symposium in Nashville. Who knows? Maybe he’ll get to see the homeless man who caught his eye a few years ago. Only this time Dr. Geller will be prepared to help that man’s dog with some basic medical care.

BOX: Joining the Coalition

The National Law Center on Homelessness and Poverty estimates that 3.5 million Americans experience homelessness each year, and up to 10% of those people have dogs or cats. Street Dog Coalition clinics are typically run at or near shelters for homeless people and other places where the homeless congregate. Veterinarians interested in setting up an agreement with the Street Dog Coalition are given the following items to get started:

- A $1 million general liability insurance policy
- A 15 x 20–foot canvas medical tent
- A $500 startup stipend for supplies and medication
- Up to $500 startup stipend for follow-up care and spay-neuter vouchers for use at a collaborating veterinary clinic
- A $500 annual stipend for ongoing medical supplies
- Up to a $500 annual stipend for follow-up care and spay-neuter vouchers
**Product Spotlight**

A look at some of the latest and greatest products in veterinary medicine.

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**NEXGARD (AFOXOLANER) CHEWABLES**

**Marketed By:** Merial, Inc.

NexGard (afloxolane) is a soft, beef-flavored chew that is indicated to kill both fleas and ticks and to keep killing for a whole month. It has been proven safe and effective for use in dogs and puppies 8 weeks of age or older, weighing 4 pounds or more.

**Dosage Form:** Soft, beef-flavored chew

**Important Safety Information:** NexGard is for use in dogs only. The most frequently reported adverse reactions included pruritus, vomiting, dry/flaky skin, diarrhea, lethargy, and lack of appetite. The safe use of NexGard in pregnant, breeding, or lactating dogs has not been evaluated. Use with caution in dogs with a history of seizures. See full prescribing information on page 1.

**For More Information:** nexgardfordogs.com

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**GALLIPRANT**

**Marketed By:** Elanco Animal Health

Galliprant (grapiprant tablets) is a first-in-class piprant (a non–COX-inhibiting prostaglandin receptor antagonist) indicated for the control of pain and inflammation associated with osteoarthritis (OA) in dogs. Galliprant blocks the prostaglandin EP4 receptor, the primary mediator of canine OA pain and inflammation, but does not inhibit the production of many housekeeping prostanoids that maintain homeostatic functions.

**Dosage Form:** 20-mg, 60-mg, and 100-mg tablets

**For More Information:** elanco.us

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**SOLLIQUIN**

**Marketed By:** Nutramax Laboratories

Solliquin is a behavioral health supplement that aims to help support normal behavior and facilitate a calming effect for anxious pets. The product, which contains the amino acid L-theanine, Magnolia and Phellodendron extracts, and whey protein concentrate, is intended for use as part of a multimodal plan to treat pet anxiety.

**Dosage Form:** Soft chews for dogs and cats; chewable tablets for medium to large dogs

**For More Information:** solliquin.com

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**VET25 AND VET30**

**Marketed By:** SunTech Medical

The Vet25 monitor is designed for monitoring blood pressure in either the examination or operating room. The Vet30 combines blood pressure technology with pulse oximetry and temperature capabilities for continuous monitoring before, during, and after procedures.

**For More Information:** suntechmed.com

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**ALFAXAN**

**Marketed By:** Jurox

Alfaxan (alfaxalone 10 mg/mL) is indicated for use in dogs and cats for both induction and maintenance of anesthesia and for induction of anesthesia followed by maintenance with an inhalant anesthetic. Alfaxalone is a neuroactive steroid molecule with central effects. It is a progesterone analogue but does not bind to sex hormone, glucocorticoid, or mineralocorticoid receptors.

**Dosage Form:** Intravenous injection

**For More Information:** alfaxan.com

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**RESCUE**

**Marketed By:** Virox Animal Health

Accelerated hydrogen peroxide is the primary ingredient in Rescue, a line of nonabrasive disinfectants designed for use on hard, nonporous surfaces such as non-food contact countertops, cages, exam tables, kennels, and animal equipment and devices. Rescue also reduces odor-causing bacteria, leaving surfaces smelling clean and fresh.

**Available Formats:** Concentrate, ready-to-use liquid, wipes, and high-level disinfectant

**For More Information:** viroxanimalhealth.com
Choose a product that offers forgiveness

Because life happens, choose Advantage Multi® for Dogs. Heartworm protection that forgives if clients forget to apply on the same day every month.*

Broad-Spectrum parasite protection in a convenient monthly topical application

*If you forget and go over 30 days between treatments, just treat immediately and resume your monthly schedule.

CAUTION: Federal (U.S.A.) law restricts Advantage Multi® for Dogs (imidacloprid + moxidectin) to use by or on the order of a licensed veterinarian. WARNING: DO NOT ADMINISTER THIS PRODUCT ORALLY. For the first 30 minutes after application ensure that dogs cannot lick the product from application sites on themselves or other treated animals. Children should not come in contact with the application site for two (2) hours after application. See Contraindications, Warnings, Human Warnings, and Adverse Reactions, for more information.

CONTRAINDICATIONS: Do not use this product on cats.

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¹ Data on file at Merial.