Clinical News and Business Insight in Companion Animal Health Care

CONFERENCES

NY VET

Osteoarthritis in Cats

According to Rebecca Stepien, DVM, 2018 Midwest Veterinary Conference stage cardiac disease in cats. At the available diagnostic tools to detect and its current form involves collecting, cell transfer (ACT) is an emerging form of cellular therapy that in

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ACVP

Test-driving CARs to Treat Canine Lymphoma

According to Nicola J. Mason, PhD, BVetMed, DACVIM, associate professor of medicine and pathobiology at the University of Pennsylvania School of Veterinary Medicine in Philadelphia, adoptive cell transfer (ACT) is an emerging form of cellular therapy that in

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MVC

Advances in Feline Heart Disease Diagnosis

Cats are more adept than dogs at hiding clinical signs of heart disease, according to Rebecca Stepien, DVM, DACVIM, clinical professor of cardiology at the University of Wisconsin School of Veterinary Medicine. That's why it is important to use multiple available diagnostic tools to detect and stage cardiac disease in cats. At the 2018 Midwest Veterinary Conference

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FEATURE

Current Options for Managing Canine Osteoarthritis

David Dycus, DVM, MS, CCRP, DACVS-SA, is on a mission. He wants to help his fellow veterinarians understand that managing canine osteoarthritis (OA) is not a matter of simply prescribing a pain reliever and an anti-inflammatory and sending patients on their way. Instead, he said, managing this chronic, painful condition requires a patient-specific, multipronged approach.

"At the end of the day, it's all about keeping patients comfortable so they can stay active, maximize range of motion, and maintain lean body weight," said Dr. Dycus, an orthopedic staff surgeon at Veterinary Orthopedic & Sports Medicine Group in Annapolis Junction, Maryland, and cofounder/codirector of the Veterinary Sports Medicine and Rehabilitation Institute. "If our patients aren't comfortable, they're not going to be active." And with inactivity, he said, comes weight gain, stiffness, and loss of range of motion.

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CLINICAL FOCUS

THERAPEUTICS

Laser Therapy Today

Documentation of light therapy dates back 3000 years, but it wasn’t until about 100 years ago that Albert Einstein theorized the possibility of a LASER (light amplification by the stimulated emission of radiation)—yet his theories did not come to fruition until 1960, when the first working laser light was produced. Since then, lasers, laser light, and light-emitting diodes have become integral to everyday life, from communication and entertainment uses to industrial and military applications.

The medical front is rife with life-changing advances attributed to lasers, including treatment of disfiguring dermatologic conditions, ophthalmologic diseases, dental and oral maladies, prostate disease, neurologic and orthopedic conditions, and intrathoracic and abdominal conditions.

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OPHTHALMOLOGY

Vision in Dogs and Cats

Every now and then veterinarians are asked about animal vision: “Are dogs truly color blind?” or “Do cats have superIOR night vision?” or “Who sees better, my dog or my cat?” Vision is an extremely complex sense that is influenced by various elements, differs significantly among species, and can be tested using many methodologies. Thus, there is no easy way to answer these questions.

It’s true that some animals, including cats and dogs, may be partially color blind, but certain aspects of their vision are superior to that of humans. Not only is it interesting to imagine how your patients see the world, but having a better understanding of their vision can positively influence, for example, the choice of lighting you use in your office.

Although this review is not intended to offer an exhaustive discussion of the topic, it does focus (pun intended) on select aspects of vision in our patients.

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Important Safety Information: For use in cats only. Animals presenting with severe ketoacidosis, anorexia, lethargy, and/or vomiting should be stabilized with short-acting insulin and appropriate supportive therapy until their condition is stabilized. As with all insulin products, careful patient monitoring for hypoglycemia and hyperglycemia is essential to attain and maintain adequate glycemic control and to prevent associated complications. Overdosage can result in profound hypoglycemia and death. Progestogen and glucocorticoid use should be avoided. PROZINC insulin is contraindicated in cats during episodes of hypoglycemia and in cats sensitive to protamine zinc recombinant human insulin or any other ingredients in the PROZINC product.

The glucose nadir from a 9-hour blood glucose curve was between 80 and 150 mg/dL and clinical signs of hyperglycemia such as polyuria, polydipsia, and weight loss were improved.

Monitoring for hypoglycemia and hyperglycemia is essential to attain and maintain (protamine zinc recombinant human insulin) ProZinc®. NADA 141-297, Approved by FDA.

Body weight, or concomitant medication, or if the cat develops concurrent infection, further adjustments in the dosage may be necessary with changes in the cat's diet, and, if needed, a dose reduction.

Adequate glycemic control and to prevent associated complications. Overdosage can result in hypoglycemia. An animal with signs of hypoglycemia should be treated with short-acting insulin and appropriate supportive therapy. (See Cat Owner Information Sheet). Use of this product, even at established doses, has been reported in the effectiveness analysis. The patients included various purebred and mixed breed cats ranging in age from 3 to 19 years and in weight from 4.6 to 20.8 pounds. Of the cats that completed the effectiveness study, one of which had hypoglycemia. Four cats had received ProZinc insulin for less than one clinic sign (polyuria, polydipsia, or body weight). Based on this definition, 115 of 151 cats (76.2%) were considered successful. Blood glucose cure means decreased from 415.3 mg/dL on Day 0 to 203.2 mg/dL by Day 5, and the mean blood glucose nadir decreased from 407.9 mg/dL on Day 0 to 142.4 mg/dL on Day 45. Four cats were diagnosed with diabetic ketoacidosis during the study. Two were euthanized due to poor response to treatment. Five other cats were euthanized during the study, one of which had hypoglycemia. Four cats had received ProZinc insulin for less than a week and were euthanized due to worsening concurrent medical conditions. The following additional clinical observations or diagnoses were reported in cats during the effectiveness field study: vomiting, lethargy, cystitis/hematuria, upper respiratory infection, dry coat, hair loss, ocular discharge, abnormal vocalization, black stool, and rapid breathing.

Extended Use Field Study

Cats that completed the effectiveness study were enrolled into an extended use field study. In this study, 145 cats received ProZinc insulin for up to an additional 136 days. Adverse reactions were similar to those reported during the 45-day effectiveness study and are listed in order of decreasing frequency: vomiting, hypoglycemia, anorexia, poor appetite, diarrhea, lethargy, cystitis/hematuria, and weakness. Twenty cats had signs consistent with hypoglycemia as described as sluggish, lethargic, unsteady, weak, seizures, trembling, or dazed. Most of these were treated by the owner or veterinarian with oral glucose supplementation or food; others received intravenous glucose. One cat had a serious hypoglycemic event associated with seizures and blindness. The cat fully recovered after supportive therapy and finished the study. All cases of hypoglycemia resolved with appropriate therapy and if needed, a dose reduction.

Fourteen cats died or were euthanized during the extended use study. In two cases, continued use of insulin despite anorexia and signs of hypoglycemia contributed to the deaths. In one case, the owner decided not to continue therapy after a presumed episode of hypoglycemia. The next were due to concurrent medical conditions or worsening of the diabetes mellitus.

To report suspected adverse reactions, or to obtain a copy of the Material Safety Data Sheet (MSDS), call 1-866-638-2226.

Information for Cat Owners: Please refer to the Cat Owner Information Sheet for more information about ProZinc insulin. ProZinc insulin, like other insulin products, is not free from adverse reactions. Owners should be advised of the potential for adverse reactions and be informed of the associated clinical signs. Potential adverse reactions include hypoglycemia, insulin antagonism/resistance, rapid insulin metabolism, insulin-induced hyperglycemia (Somogyi Effect), and local or systemic reactions. The most common adverse reaction observed is hypoglycemia. Signs may include: weakness, depression, behavioral changes, muscle twitching, and amnestic episodes. In severe cases of hypoglycemia, seizures and coma can occur. Hypoglycemia can be fatal if an affected cat does not receive prompt treatment. Appropriate veterinary monitoring of blood glucose, adjustment of insulin dose and regimen as needed, and stabilization of diet and activity help minimize the risk of hypoglycemic episodes. The attending veterinarian should evaluate other adverse reactions on a case-by-case basis to determine if an adjustment in therapy is appropriate, or if alternative therapy should be considered.

Effectiveness: A total of 187 client-owned cats were enrolled in a 45-day field study, with 176 receiving ProZinc insulin. One hundred and fifty-one cats were included in the effectiveness analysis. The patients included various purebred and mixed breed cats ranging in age from 3 to 19 years and in weight from 4.6 to 20.8 pounds. Of the cats included in the effectiveness analysis, 101 were castrated males, 49 were spayed females, and 1 was an intact female.

Cats were started on ProZinc insulin at a dose of 0.1-0.3 IU/lb (0.2-0.7 IU/kg) twice daily. Cats were evaluated at 7, 14, 30, and 45 days after initiation of therapy, and the dose was adjusted based on clinical signs and results of 9-hour blood glucose curves on Days 7, 14, and 30. Effectiveness was based on successful control of diabetes, which was defined as improvement in at least one blood glucose variable (glucose curve means steady, or fluctuating, and at least one clinical sign (polyuria, polydipsia, or body weight). Based on this definition, 115 of 151 cats (76.2%) were considered successful. Blood glucose cure means decreased from 415.3 mg/dL on Day 0 to 203.2 mg/dL by Day 5, and the mean blood glucose nadir decreased from 407.9 mg/dL on Day 0 to 142.4 mg/dL on Day 45. Mean fructosamine values decreased from 305.9 mmol/L on Day 0 to 280.2 mmol/L on Day 45. Cats that completed the effectiveness study were enrolled in an extended use field study. The mean fructosamine value was 342.0 mmol/L after a total of 181 days of ProZinc therapy.

How Supplied: ProZinc insulin is supplied as a sterile injectable suspension in 10-mL multidose vials. Each mL of ProZinc product contains 40 IU recombinant human insulin.

Storage Conditions: Store in an upright position under refrigeration at 36-46°F/2-8°C. Do not freeze. Protect from light.

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DEALING WITH COLLAPSE IN DOGS

“COLLAPSE IN DOGS IS one of the most frustrating things we see in the emergency room,” says Liz Rozanski, DVM, associate professor of emergency and critical care at the Cummings School of Veterinary Medicine at Tufts University. “And collapse is, unfortunately, common.”

The primary factor in helping these pets is to have owners bring them to the hospital as soon as possible, because time is of the essence. “Most cases of collapse respond well to therapy,” Dr. Rozanski says. “We just have to figure out what we’re dealing with.” She advises veterinarians to consider whether the pet may have gotten into a poison, is bleeding internally, has pericardial effusion, is suffering from heat stroke, or has hypertension or hypotension. “Check the major body systems—the heart, brain, and lungs—and see if there’s an abnormality there,” she says. “Then start thinking about how you can correct that abnormality by giving fluids, oxygen, or a blood transfusion or by removing fluids.”

THOUGHTFUL FLUID ADMINISTRATION

“DON’T BE AFRAID OF FLUIDS,” says Deborah Silverstein, DVM, DACVECC, associate professor of critical care at the University of Pennsylvania School of Veterinary Medicine. “They are your friend. But they can also lead to adverse effects.”

It shouldn’t be a scary process to administer fluids, Dr. Silverstein says, but carefully evaluating the patient’s initial presentation in terms of cardiovascular stability and hydration status is important, and don’t forget you have to repeatedly reevaluate those to avoid any adverse effects.

“Trying not to give too much fluid is probably the most important consideration,” Dr. Silverstein says. “But at the same time you need to be sure perfusion is adequate so the organs don’t suffer from oxygen deficits and subsequent injury.”

All in all, she recommends that veterinarians be “cautiously judicious” in their choices of fluids and monitor patients frequently for any changes or potential complications.

FEAR FREE FOR CATS: SIMPLE STRATEGIES

Lisa Radosta, DVM, DACVB, owner of Florida Veterinary Behavior Service in West Palm Beach, offers a few easy and inexpensive suggestions for practices that want to start implementing feline Fear Free tactics. “The first thing is to use pheromone diffusers and sprays,” she says. “Will they work on every cat? No, but they will help many cats to be calmer in the practice.”

Second, she advocates minimizing or eliminating the amount of time that stressed cats spend in the waiting room. “Having a separate cat waiting room is fantastic, but we can’t all do that,” Dr. Radosta acknowledges. Instead, she suggests that practices have cats and their owners wait in the car until an exam room becomes available.

“Finally,” she says, “I know we’re all running 24/7, but what we can do as doctors is take a deep breath and consider examining our stressed feline patients in their carriers or sitting on the floor and putting that cat on our lap.” By simply rethinking how you examine stressed feline patients, you are implementing a Fear Free technique.

WITH EYE PROBLEMS, RAPID INTERVENTION IS KEY

“ISSUES CAN TURN south in eyeballs really, really quickly,” says Jennifer Welser, DVM, DACVO, chief medical officer of BluePearl Veterinary Partners, “so rapid intervention is key.”

When it comes to eyes, several diseases require immediate attention, Dr. Welser explains. It is much better to act too quickly and too aggressively than to miss the boat, because these animals can lose vision or the eyes themselves. “Even if you’re wrong,” she says, “you can always justify the fact that you treated it aggressively.”

And while it might sound simple to get clients to understand that, Dr. Welser says it can be tricky sometimes to get clients to come in to the practice when there is a problem with their pet’s eye.

HOW OFTEN SHOULD PETS RECEIVE DENTAL EXAMS?

GENERALLY SPEAKING, SAYS Vickie Byard, CVT, VTS (Dentistry), dentistry specialist at PetED Veterinary Education and Training Resources, most dogs and cats should receive annual dental examinations. “I like to tailor it according to how much oral care the pet owner is able to do at home,” Byard says.

Larger-breed dogs can wait a bit longer between dental exams, she notes, while smaller breeds should probably come in every 6 to 9 months, “especially if they’re high strung and their owners can’t do any home care.”

MAKING THE MOST OF ELECTROCARDIOGRAMS IN ANESTHESIA MONITORING

BASIC MONITORING FOR every veterinary patient under anesthesia includes an electrocardiogram (ECG). But while they give us a lot of information, Gregg M. Grifenhagen, DVM, MS, DACVAA, anesthesiologist and clinical instructor at Colorado State University, says we start to ignore them over time. He offers a simple 3-step approach to better understand an ECG:
• Look at the P waves.
• Look at the QRS complexes.
• Ask: Are they associated? Are they wide?

With monitoring today providing so much data, it becomes imperative to be able to determine quickly what is important and what needs to be done. “[This approach to the ECG] gives you the basic information to very easily look and say, ‘Here’s what I see, here’s what I think should treat it,’ and then move on,” he says.
IMPORTANT SAFETY INFORMATION:
For oral use in dogs only. Not for human use. Keep out of reach of children. If accidentally ingested by humans, contact a physician immediately.

The most commonly reported side effects were vomiting, loss of appetite, diarrhea, excessive salivation, agitation, tiredness, vocalization, confusion, increased water consumption, weight loss, weakness, fever, panting, and reversible changes in skin color (flushing or bright pink). Abnormal gait, seizures or tremors, as well as liver enzyme elevations, kidney failure, blood in urine and urine retention have been reported. In some cases death, including euthanasia has been reported. Sudden death was sometimes preceded by vocalization or collapse.

Instances of dogs chewing through closed vials of PROIN and eating the vial contents have been reported, in some cases resulting in overdose. Keep the product in a secured storage area out of the reach of pets in order to prevent accidental ingestion or overdose, as dogs may willingly consume more than the recommended dosage of PROIN Chewable Tablets. Contact your veterinarian immediately if the dog ingests more tablets than prescribed or if other pets ingest PROIN Chewable Tablets.

PROIN may cause elevated blood pressure and should be used with caution in dogs with pre-existing heart disease, high blood pressure, liver disease, kidney insufficiency, diabetes, glaucoma, and other conditions associated with high blood pressure.

The safe use of PROIN in dogs used for breeding purposes, during pregnancy or in lactating bitches, has not been evaluated. Contact your veterinarian if you notice restlessness or irritability, loss of appetite, the incontinence persists or worsens, or any other unusual signs. See prescribing information for complete details regarding adverse events, warning and precautions or visit prnpharmacal.com.
Penn Vet Launches Behavior Telemedicine App

THE RECENTLY LAUNCHED PENN VET Behavior App is a consultation service available to veterinarians around the world. Developed in partnership with Connect For Education and the University of Pennsylvania School of Veterinary Medicine (Penn Vet) Center for the Interaction of Animals and Society, the platform allows veterinarians to consult directly with Penn Vet board-certified behavior specialists.

A client-facing component allows pet owners to upload videos of their pets for evaluation, access educational resources that have been curated by Penn Vet specialists, and participate in chats with experts.

“It’s not the same service as a full behavior consult at the hospital would be, but it’s going to meet a need that isn’t being met for a lot of pet owners,” explained Carlo Siracusa, DVM, PhD, MS, who directs the behavior service at Penn Vet’s Ryan Hospital. The pilot launch, underway now, allows invited veterinarians to use the portal for 6 months without paying a fee. A wider rollout is expected later this year.

FDA Reissues Warning About Sileo

THE FDA HAS REISSUED AN ADVISORY to veterinarians and pet owners about the risk of accidental overdose for dogs prescribed Sileo, a prescription gel given to dogs orally for the treatment of noise aversion. From the product’s launch in May 2016 through May 16, 2018, the FDA received 54 adverse event reports involving Sileo overdoses in dogs—the result of the product’s ring-stop mechanism not properly locking at the intended dose. Within the year that the FDA published its original Animal Drug Safety Communication on the issue, an additional 26 accidental overdoses in dogs were documented. To date, no deaths have been reported. The FDA urges all prescribing veterinarians and users to be aware of the potential for accidental overdose if the syringe is not locked properly before dosing and administering.

Disposing of Pet Pharmaceuticals: A Teachable Moment

MORE THAN 60% OF VETERINARY care professionals do not advise their clients on how to dispose of pet pharmaceuticals and personal care products (PPCP), say the authors of a new survey study from Oregon State University (OSU). While this finding is certainly troublesome with regard to environmental stewardship, the authors believe it also presents veterinarians with a great opportunity to educate their clients.

The research team surveyed 191 environmental educators and veterinary health care professionals, all of whom owned pets, regarding their methods of disposing of human and pet PPCP. Nearly half (46%) said they disposed of unneeded products by simply throwing them out. The research also revealed that 61% of the 103 veterinary professionals surveyed did not share information about proper PPCP disposal with clients. And the 39% who did bring up the topic did so only with about 1 in 5 clients.

According to Sam Chan, a watershed health expert with the Oregon Sea Grant program at OSU, chemicals from PPCP, such as anti-inflammatories, antidepressants, and antibiotics, are being found more commonly in groundwater and surface water—in part because of the growing number of pets in American homes.

“PPCP are used by almost everyone,” Chan said. “Most people tend to throw extra pills or personal care products into the trash and, in fewer instances, flush them down the drain. Most wastewater treatment plants are not able to completely deactivate many of the compounds they include.”

The investigators propose that veterinarians can help reduce the amount of watershed contaminants immensely by educating pet owners about proper disposal of PPCP, including the following:

- Do not flush unused medications down the toilet, unless recommended by the FDA.
- Crush medications or dissolve them in water, then mix them with an absorbent material—such as kitty litter, dirt, or sawdust. To prevent leakage, place the material in a sealable plastic bag before throwing it in the garbage.
- Advise clients about any local or state hazardous waste collection programs or pharmacies that will take back unused medications.
- Before discarding prescription bottles, remove all personal identification information.

Dispensing of Pet Pharmaceuticals: A Teachable Moment

By Amanda Carrozza

Referece


CDC Unveils New Rapid Rabies Detection Test

By Amanda Carrozza

THE CENTERS FOR DISEASE CONTROL and Prevention (CDC) announced that its researchers have developed a test that can diagnose rabies infections more easily and precisely than current methods. The new test, designed for use in animals, is being celebrated for its ability to deliver accurate results in 2 hours, allowing doctors to make more informed treatment decisions. The CDC’s announcement of the LN34 test was accompanied by results of the largest study ever to validate use of a real-time polymerase chain reaction test to diagnose rabies in animals.

During the study, about 3000 brain samples from 60 mammal species—including dogs, raccoons, skunks, foxes, and bats—from areas in the Americas, Europe, Africa, and Asia were assessed. Of these animals, 1000 were known to be infected with the rabies virus. The LN34 test correctly identified all direct fluorescent antibody (DFA)-positive samples as positive. It also produced definitive findings for 80 samples deemed inconclusive or untestable by DFA, 29 of which were positive for rabies. Of the 3000 samples tested, the LN34 test identified 1 false-negative and 11 false-positive DFA test results. Only 1 sample was indeterminate using both tests.

The results, the investigators said, demonstrate the “reliability and robustness of the LN34 assay” and support a role for the test in improving rabies diagnostics and surveillance.

To date, the DFA test is regarded as the gold standard for postmortem rabies diagnostics and is the only internationally approved test. However, according to the CDC, the DFA “can only be interpreted by laboratory workers with special skills, extensive training, and a specific type of microscope.” The test can also only be run on fresh brain tissue samples that have been kept cold. As such, it is difficult to use and access in resource-poor areas.

By contrast, researchers found that the LN34 test “was able to detect minuscule amounts of rabies virus genetic material, even in samples so old they had liquefied. Moreover, the condition of the sample did not affect the test’s accuracy.”

Reference

Pet owners already have a lot to remember. Give them one less thing to forget.

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

IMPORTANT SAFETY INFORMATION: BRAVECTO has not been shown to be effective for 12-weeks’ duration in puppies or kittens less than 6 months of age. BRAVECTO Chew: The most common adverse reactions recorded in clinical trials were vomiting, decreased appetite, diarrhea, lethargy, polydipsia, and flatulence. BRAVECTO is not effective against lone star ticks beyond 8 weeks of dosing. BRAVECTO Topical Solution for Dogs: The most common adverse reactions recorded in clinical trials were vomiting, hair loss, diarrhea, lethargy, decreased appetite, and moist dermatitis/rash. BRAVECTO is not effective against lone star ticks beyond 8 weeks of dosing. For topical use only. Avoid oral ingestion. Use caution in dogs with a history of seizures. Seizures have been reported in dogs receiving fluralaner, even in dogs without a history of seizures. BRAVECTO Topical Solution for Cats: The most common adverse reactions recorded in clinical trials were vomiting, itching, diarrhea, hair loss, decreased appetite, lethargy, and scales/ulcerated lesions. BRAVECTO is not effective against American dog ticks beyond 8 weeks of dosing. For topical use only. Avoid oral ingestion. The safety of BRAVECTO has not been established in breeding, pregnant and lactating cats. Use with caution in cats with a history of neurologic abnormalities. Neurologic abnormalities have been reported in cats receiving BRAVECTO, even in cats without a history of neurologic abnormalities. See full Prescribing Information on the following page.
**BRAVECTO® (Fluralaner topical solution) for Dogs**

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

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

**Indications:**
Braveo kills adult fleas and is indicated for the treatment and prevention of flea infestations (Ctenocephalides felis) and the treatment and control of tick infestations (Ixodes scapularis (black-legged tick), Dermacentor variabilis (American dog tick), and Amblyomma americanum (lone star tick)) for 12 weeks in dogs and puppies 6 months of age and older, and weighing 4.4 pounds or greater.

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

**Contraindications:**
- There are no known contraindications for the use of the product.
- **Warnings:**
  - Not for human use. Keep this and all drugs out of the reach of children. Do not contact or allow children to contact the application site until dry, keep the product in the original packaging until use, and in order to prevent children from getting direct access to the product. Do not eat, drink or smoke while handling the product. Wash hands thoroughly with soap and water immediately after use of the product.

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

**Adverse Reactions:**
- In a well-controlled U.S. field study, which included 204 dogs (224 dogs were administered Bravecto every 12 weeks and 70 dogs were administered an oral active control every 4 weeks and were provided with a tick collar); there were no serious adverse reactions. All potential adverse reactions were recorded in dogs treated with Braveo over a 122-day period and in dogs treated with the active control over an 84-day period. The most frequently reported adverse reaction in dogs in the Braveo and active control groups was vomiting.

**Percentage of Dogs with Adverse Reactions in the Field Study**

<table>
<thead>
<tr>
<th>Adverse Reaction (AR)</th>
<th>Bravecto Group: Percent of Dogs with the AR During the 182-Day Study (n=224 dogs)</th>
<th>Active Control Group: Percent of Dogs with the AR During the 84-Day Study (n=70 dogs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vomiting</td>
<td>7.1%</td>
<td>14.3%</td>
</tr>
<tr>
<td>Decreased Appetite</td>
<td>6.7%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>4.9%</td>
<td>2.9%</td>
</tr>
<tr>
<td>Lethargy</td>
<td>5.4%</td>
<td>7.1%</td>
</tr>
<tr>
<td>Polydipsia</td>
<td>3.5%</td>
<td>4.3%</td>
</tr>
<tr>
<td>Tautulence</td>
<td>3.0%</td>
<td>0.0%</td>
</tr>
</tbody>
</table>

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

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

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

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

**WARNINGS**

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

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

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

<table>
<thead>
<tr>
<th>Adverse Reaction (AR)</th>
<th>Bravecto Group: Percent of Cats with the AR During the 105-Day Study (n=224 cats)</th>
<th>Control Group: Percent of Cats with the AR During the 84-Day Study (n=87 cats)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vomiting</td>
<td>6.3%</td>
<td>6.0%</td>
</tr>
<tr>
<td>Alopexia</td>
<td>4.1%</td>
<td>2.0%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>2.7%</td>
<td>11.0%</td>
</tr>
<tr>
<td>Lethargy</td>
<td>2.7%</td>
<td>2.0%</td>
</tr>
<tr>
<td>Decreased Appetite</td>
<td>0.9%</td>
<td>0.8%</td>
</tr>
<tr>
<td>Most Common Reactions</td>
<td>0.9%</td>
<td>0.0%</td>
</tr>
</tbody>
</table>

In the field study, two dogs treated with Braveo with no prior history of seizures each experienced a seizure. One dog had two seizures a day apart about 18 days after its first dose. The dog was started on antiepileptic medication and had no additional seizures during the study. A second dog had a seizure 76 days after its first dose and 3 days after starting fluralaner; even in dogs without a history of seizures. Braveo has not been shown to be effective for 12-weeks duration in puppies less than 6 months of age. Braveo is not effective against Amblyomma americanum ticks beyond 8 weeks after dosing.

**Contraindications:**
- There are no known contraindications for the use of the product.
Diagnostic and Treatment Choices for Canine UTI in Denmark
By Natalie Stiwell, DVM, MS, PhD

DANISH RESEARCHERS RECENTLY performed a prospective study examining diagnostic methods and treatment choices for urinary tract infection (UTI) in companion animal practice. Between May 2014 and November 2016, 151 dogs presenting to 52 veterinary practices throughout Denmark were enrolled in the study. All dogs presenting for 1 or more clinical signs consistent with UTI were eligible; those with systemic or chronic disease or those given antibiotics within 3 weeks before presentation were excluded. Fifty-eight breeds were represented, with a mean age of 6 years and mean weight of 21.7 kg. Most dogs were female (73%). The most commonly reported clinical sign was pollakiuria (80%) occurring for a median duration of 3.3 days before consultation. During consultation, in-house diagnostics performed on urine samples included urine dipstick analysis, microscopy, sediment staining, quantitative bacterial culture (QBC), and antibiotic susceptibility testing (AST). QBC and AST were also performed at the University of Copenhagen reference laboratory for a subset of cases. In addition, pet owners recorded clinical signs and treatment administration for 10 days after consultation. The investigators examined whether practitioners made the appropriate decision to treat for UTI empirically and after receiving QBC results. They also analyzed whether practitioners selected an appropriate first-line antibiotic for treatment (amoxicillin or potentiated sulfonamides) based on AST results. The most commonly utilized in-house diagnostic procedures were urine dipstick (99%), microscopy (80%), and QBC (56%). Veterinarians tentatively diagnosed UTI in 132 cases (87%) and empirically treated 119 dogs (79%) with antibiotics. Reference lab QBC results subsequently confirmed UTI diagnosis for 77 dogs (51%), including 74 already receiving empiric treatment. Of the 74 dogs negative for UTI, 55 (74%) received empiric antibiotic therapy. Overall, veterinarians appropriately decided whether to prescribe antibiotics in 62% (93/151) of cases. The use of in-house microscopy, but not QBC, significantly increased the likelihood of appropriate treatment selection. Compared with the reference lab QBC, in-house microscopy and in-house QBC were 65% and 77% accurate, respectively, at detecting UTI. AST results showed that appropriate first-line antibiotics were selected in 36% of confirmed UTI cases, while second-line agents were prescribed in 57% of cases. Nineteen-percent of bacterial isolates were resistant to 1 or both first-line antibiotics. Owner diaries were returned for 101 dogs, 53% of which were confirmed positive UTI cases. The median time from consultation to resolution of clinical signs was 2 days for UTI and non-UTI cases; clinical signs persisted in 7% of cases 10 days after consultation. The authors acknowledged that the decision to treat UTI is complex, as delaying treatment until culture and antibiotic susceptibility results are available is not always feasible. Nevertheless, the investigators determined that overtreatment of UTI is a common issue in Danish veterinary practices.


Cages, Stress, and Upper Respiratory Infection in Shelter Cats

WITH INCIDENCE RATES as high as 30%, feline upper respiratory infection (URI) is one of the leading disease concerns in animal shelters. Because of its prevalence and ability to spread quickly, URI is also believed to be a common reason for feline euthanasia in shelter environments. With the understanding that URI could be linked to stress, and that shelter animals are prone to increased levels of stress, researchers from the University of California, Davis conducted a study to assess whether physical modifications made in animal shelters would impact URI rates. The study investigators partnered with 9 animal shelters across North America and collected data from August 1, 2008, through July 31, 2009. Shelter staff were responsible for recording daily data about their feline populations and completed surveys about the cats’ environments. To determine the monthly URI rate, the total of new cases was divided by the days at risk for URI. Over the course of the study, 18,373 adult cats were included, with 210,987 days at risk and 31,924 URI days recorded. After analyzing the data, the investigators determined that to minimize stress and cases of URI, cats required about 8 square feet of floor space in their cages. This is double the 4 square feet that investigators found to be the average. Cats that were moved between cages fewer than 2 times in the first week of arrival were also less likely to contract URI. The authors attributed this to stress levels associated with frequent changes in housing. “Our study demonstrated that a disease we thought was almost inevitable in shelters is absolutely preventable, and prevention could be as simple as just giving the cat enough space,” Kate Hurley, DVM, study author and director of the UC Davis Koret Shelter Medicine Program, said. “By making these changes, shelters can make cats happier, lower staff stress by making their jobs easier, and increase adoptions and shelter success in saving lives.”


Pet Obesity: Good News and Bad News

THE ASSOCIATION FOR Pet Obesity Prevention’s 10th annual survey revealed a rather discouraging, but not entirely unexpected, statistic. Despite increased attention to the issue and a shift toward feeding “all-natural” and “grain-free” diets, pet obesity in the United States remains a growing problem. In 2017, 60% of cats and 56% of dogs were obese. The survey results weren’t all disappointing, however. When asked about encouraging weight loss, 58% of pet owners and 54% of veterinary professionals reported that they had tried to help their pets lose weight, largely through low-calorie and weight-loss diets combined with increased exercise. When asked what prevented them from exercising their dogs, the most common response among both groups was “too busy,” followed by behavior issues, inadequate access to exercise areas, and physical limitations of the owner and pet. One of the most interesting findings was the notable difference in how pet owners and veterinary professionals perceived diets and ingredients. When asked whether low- or no-grain diets are healthier for dogs, 46% of pet owners said yes and 63% of veterinary professionals said no. Similarly, 63% of pet owners said corn was not healthy for dogs, but 50% of veterinary professionals said no. Pet owners were particularly confused about raw food diets. Most veterinary professionals (72%) reported that raw diets were not healthier for cats and dogs. The most common response among pet owners was that they simply didn’t know whether raw diets were any healthier (45%). This was up from last year’s results, in which 35% of pet owners reported uncertainty. One area on which both groups agreed was that commercial pet food is better than it was 10 years ago (63% of pet owners and 76% of veterinary professionals). The survey results reiterated that veterinarians and their teams play a pivotal role not only in identifying obese or at-risk patients but also in offering clients actionable advice on how to help their pets lose weight and maintain healthy lifestyles—and that there is room for improvement. Among pet owners, 48% said their veterinarian failed to recommend a maintenance or routine diet for their pet. This is in line with responses from veterinary professionals, only 50% of whom said they offered maintenance pet food recommendations. When pet owners were asked where they receive the best dietary recommendations for their animals, “veterinary professionals” was the most popular choice (57%), followed by online searches (52%).
Osteoarthritis in Cats

Diagnosing joint disease in feline patients can be difficult, but recognizing and managing this chronic, painful condition is important for achieving optimal quality of life.

By Laurie Anne Walden, DVM, ELS

OA in cats is underdiagnosed, said Dr. Little, co-owner of 2 feline practices in Ottawa, Canada. “[Cats are] often really good at masking their signs of orthopedic disease,” she noted. In addition, the disease is often bilateral, so gait abnormalities are harder to spot than they are with unilateral disease. Understanding these barriers to symptom recognition is a step toward making the diagnosis, she said. In cats, OA is more likely to be primary (idiopathic) than secondary. OA in dogs is more often secondary to hip dysplasia, trauma, or another cause. For veterinarians, this means that feline patients can have OA with no history of a predisposing condition.

PREVALENCE
The risk of OA “dramatically increases with age in cats,” Dr. Little said. Most senior cats have OA, she added. She recommended that veterinarians assume all cats over about 10 years of age have OA unless proved otherwise.

The most common OA locations in cats are the elbow, knee, and hip. Some cats have lumbosacral OA accompanied by spondylosis. Dr. Little noted that arthritis in this location can cause signs similar to those of ataxia. Cats sometimes present for neurologic workup when the real problem is spinal arthritis, she said. She suggested keeping this in mind when presented with an older cat with ataxia but no other signs of neurologic disease.

DIAGNOSIS
The first step in diagnosis, Dr. Little said, is having an “index of suspicion that your patients are likely to have OA.” She described a diagnostic triad of physical examination, radiography, and owner observations to help practitioners confirm the suspected diagnosis.

No specific diagnostic test exists for some feline medical conditions, she added. In these cases, a therapeutic trial can be part of the diagnostic process. “[OA] is one of the diseases in cats where response to treatment is a perfectly valid diagnostic tool,” she said.

Physical Examination
Dr. Little begins an examination of an older cat by gently palpating the entire body to locate sites of pain and then examining those areas last. “A good physical exam tip…especially with senior cats,” she said, “is to leave the difficult stuff, the painful stuff, maybe the stuff the cat doesn’t like…until the end.”

Localizing pain in cats is challenging. Dr. Little discussed several clues that a cat may be experiencing joint pain. Muscle atrophy from limb disuse can indicate chronic pain. Overgrown claws can be a sign of decreased mobility. Cats with arthritis may have unkempt fur because they do not feel well enough to groom or cannot groom themselves without pain. Cats may also overgroom painful areas, she said, suggesting that practitioners pay attention to bald spots over elbows or other joints. She also mentioned that a bald spot on the ventral abdomen of a cat with an otherwise normal coat can be a sign of bladder pain from idiopathic cystitis.

Cats with OA tend to develop joint pain and swelling. They are less likely to develop joint effusion, restricted range of motion, and crepitus, which are typical signs of OA in dogs.

Gait assessment is not always possible with cats, Dr. Little noted. She reminded the audience not to exclude OA from the differential diagnosis if a cat does not cooperate with an attempt to evaluate its gait.

Radiography
“Normal radiographs do not necessarily rule out OA in the cat,” Dr. Little said. “The problem is that cats…just have less radiographically evident pathology than dogs do.” Study results have shown that cats with OA are more likely to have cartilage changes than bone changes, she said.

Owner Observations
“We rely a lot on getting information from owners,” Dr. Little remarked. “Owners may notice changes in their senior cat. Whether they’ll report them to you is another matter.” Cat owners may think that arthritis signs are normal aging changes. She recommended asking owners specific questions about behavioral and physical changes and discussed tools that veterinarians and owners can use to uncover signs that a cat is experiencing chronic pain.

Videos and photographs of cats at home can yield important clues, she said. Videos of a cat grooming, getting in and out of the litter box, ascending and descending stairs, and jumping on and off furniture can be helpful. She also asks owners for photographs of cats resting. She pointed out that most cats at rest tuck in their forelimbs. A cat that consistently holds...
a forelimb in extension could be compensating for elbow pain, she said.

Dr. Little recommended giving owners a specific screening tool: the Feline Musculoskeletal Pain Index. This instrument was developed by the Comparative Pain Research Laboratory at the North Carolina State University College of Veterinary Medicine. It is a 17-item questionnaire in which cat owners rate their pet’s ability to perform various activities, such as jumping onto the kitchen counter, climbing stairs, stretching, grooming, interacting with family members, and using the litter box. The tool includes instructions for scoring the responses. Dr. Little suggested having owners complete the questionnaire at home, ideally before the appointment, so they will have time to think through the responses. “The worst time to ask an owner to fill out a questionnaire is…when they’re in your clinic,” she said.

Dr. Little also recommended a brochure published by the American Association of Feline Practitioners that helps owners recognize signs of pain in cats. The brochure describes behavioral changes that can indicate pain (such as hiding and becoming aggressive) and the importance of monitoring cats’ responses to therapy for chronic pain.

**TREATMENT**

The goal of treatment is to return cats to normal daily activities, Dr. Little said. Getting cats comfortable enough to interact with the family and use the litter box reliably is a worthwhile aim. Minimizing joint damage is beneficial but not necessarily the primary goal.

As with dogs, cats with OA often benefit from multimodal therapy. The choice of treatment modalities is specific to each patient and may change over time as new modalities are added, Dr. Little said.

**Diet and Nutraceuticals**

“I always prioritize weight loss,” Dr. Little said, adding that obese cats are 3 times as likely as normal-weight cats to be lame. Obesity puts extra stress on the joints and contributes to chronic low-grade inflammation, she noted.

Omega-3 fatty acid supplementation has been shown to improve activity levels in cats with arthritis, she said. Omega-3 fatty acids are available in various formulations, such as soft chews for cats, and are included in joint health diets. Dr. Little suggested checking the calorie content of joint health diets before recommending specific brands to owners of overweight (or formerly overweight) cats.

Chondroprotective agents like glucosamine/chondroitin, polysulfated glycosaminoglycan, and pentosan polysulfate are available, but Dr. Little noted that very little published research has evaluated their use in cats. Because glucosamine/chondroitin is often included in supplements and diets that also contain other products, it is difficult to know whether the combination has an effect on its own. She concluded that although there is evidence that omega-3 fatty acids and joint health diets benefit arthritic cats, there are simply very few data on the efficacy of glucosamine/chondroitin in cats.

**Drugs**

In humans and dogs with OA, nonsteroidal anti-inflammatory agents (NSAIDs) are the cornerstone of treatment, Dr. Little said. However, only a single NSAID, meloxicam, is licensed anywhere in the world for long-term use in cats— but it is not licensed for this use in North America. In the United States, meloxicam is labeled for cats only as a 1-time subcutaneous injection for controlling postoperative pain. In Canada, where Dr. Little practices, meloxicam is labeled for cats as a single subcutaneous injection and is also available as an oral suspension for short-term (up to 4 days) control of perioperative or acute musculoskeletal pain.

Using meloxicam to control chronic pain is off label in cats, so Dr. Little discussed precautions for practitioners considering it. She recommended using the lowest effective dose and stressed that the dose should be calculated according to the cat’s ideal body weight, not its actual body weight (for overweight cats). Her clinic’s medical record template includes a line for estimated ideal body weight for drug dose calculations. She also emphasized using feline-specific meloxicam formulations (such as the feline oral suspension available in Canada) for accurate dosing that is titratable to a cat’s weight.

She stressed choosing patients carefully for meloxicam administration. Meloxicam is a selective cyclooxygenase-2 (COX-2) inhibitor, so it is less likely than nonselective COX inhibitors to cause adverse effects such as kidney injury and gastrointestinal ulceration. However, patients receiving meloxicam should be stable and properly hydrated, she said. Owners must be able to watch for signs of toxicity at home and willing to bring their cats to the clinic regularly for monitoring. Dr. Little recommends reexamining cats and obtaining laboratory tests 2 to 4 weeks after beginning NSAID treatment. Cats should be rechecked periodically thereafter; the frequency depends on the patient’s condition.

Corticosteroids, antiinflammatory enzymes inhibitors, and diuretics can interact with NSAIDs, Dr. Little said. Cats receiving a corticosteroid (such as prednisolone) should not receive an NSAID at the same time.

“About two-thirds of cats with OA also have chronic kidney disease,” Dr. Little said, noting that this is a common dilemma for veterinarians. She mentioned a retrospective study conducted in Australia (where oral meloxicam is labeled for long-term use in cats) whose results showed that meloxicam administered for longer than 6 months did not exacerbate preexisting chronic kidney disease, compared with kidney disease in cats not receiving meloxicam. She pointed out that the cats in this study had stable disease, emphasizing the importance of careful patient selection. The FDA requires a warning on the package insert of the injectable product not to use meloxicam in cats with kidney dysfunction.

Dr. Little discussed 3 other drugs that can be used for pain control in cats with OA: gabapentin, buprenorphine, and tramadol. Gabapentin is probably the most commonly prescribed second-tier drug for cats that cannot receive NSAIDs, she said, although there are few published studies on its use for feline arthritis. Dr. Little typically prescribes transmucosal buprenorphine only for short-term use, either to manage breakthrough pain in a cat taking other medications or as a response-to-treatment trial in a cat with suspected OA. She does not prescribe buprenorphine for long-term use, she said, because of the potential for patients to develop tolerance to opioids. Tramadol has a bitter taste that makes it difficult to administer to cats, and it can also cause psychosis. “No matter what drug you use,” she reiterated, “these guys do need regular reevaluation.”

New drugs for chronic pain management in cats are in development, said Dr. Little. These include a monoclonal antibody and a feline-specific anti-nerve growth factor antibody.

**Feline patients can have OA with no history of a predisposing condition.**

**Environmental Modification**

Dr. Little recommends raising arthritic cats’ food and water bowls. Elevated bowls let cats with elbow arthritis eat with their elbows extended (which is less painful than holding them flexed) and give cats with hip and stifles pain a more comfortable sitting position while eating. Litter boxes should be relocated if necessary to make them easy for cats to access. Tall litter box sides may need to be cut down. Dr. Little also suggested providing steps to cats’ favorite areas (like beds and window perches) so they do not have to jump.

**Other Options**

Physiotherapy and rehabilitation can be useful for cats with arthritis, Dr. Little said. Acupuncture and laser therapy for feline OA have not been well studied, she added.

**CONCLUSION**

“This is a huge quality-of-life issue for me and a human-animal bond issue for me,” Dr. Little said. Recognizing and managing feline chronic pain makes life better for cats and for their owners.

References available at AmericanVeterinarian.com.
Test-driving CARs to Treat Canine Lymphoma

Hope—in the form of chimeric antigen receptor T-cell therapy—is on the horizon for extended remission in dogs with hematologic B-cell malignancies.

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

(continued from front cover)

manipulating, and reinfusing the patient’s own immune cells back into the body to treat cancer. Ex vivo manipulation of these cellular products frequently includes activation and expansion of either T cells or natural killer (NK) cells and genetic modification to redirect their antigenic specificity against tumor-associated antigens. Perhaps the most impressive example of ACT in human medicine today involves the use of autologous chimeric antigen receptor (CAR) T cells to treat patients with acute lymphoblastic leukemia (ALL), chronic lymphocytic leukemia (CLL) and, more recently, non-Hodgkin lymphoma (NHL).

Presenting at the American College of Veterinary Pathologists 2017 Annual Meeting in Vancouver, British Columbia, Canada, Dr. Mason described how canine CAR T cells are driving hope for effective treatment of lymphoma in dogs.

CANINE LYMPHOMA

Among the most common cancers diagnosed in dogs, lymphomas display many similarities, including clinical behavior, biology, and molecular aberrancies, to NHLs that occur in humans. Although lymphoma may affect any organ in the body, multicentric lymphoma affects the peripheral lymph nodes, spleen, liver, and bone marrow. Dogs typically present with generalized lymphadenopathy and have intermediate- to high-grade disease that is most commonly associated with malignant B cells. The most common subtype of canine NHL is diffuse large B-cell lymphoma.

Chemotherapy, the treatment of choice for most dogs with lymphoma, typically involves a doxorubicin-based, multiagent protocol. This leads to clinical remission in about 85% of dogs. Despite treatment, however, most of these dogs will relapse with lethal, drug-resistant lymphoma within 6 to 9 months of diagnosis. This suggests that our current chemotherapeutic protocols are insufficient to eliminate all neoplastic cells within the body and, as such, we routinely fail to achieve durable remission or cures with our current treatment regimens. Therefore, development of alternative treatment modalities such as immunotherapy seems to be critically important if we aim to improve on the time to progression and overall survival times in dogs with lymphoma.

WHAT IS CAR T-CELL THERAPY, AND HOW DOES IT WORK?

Over the past decade, cell-based immunotherapies have achieved unprecedented success in humans for the treatment of hematologic B-cell malignancies, including ALL, CLL, and NHL. However, their use in veterinary medicine is still in its infancy, and their effectiveness in the treatment of solid tumors has yet to be realized in either people or animals.

Most forms of ACT currently involve the use of autologous immune cells such as T cells and NK cells that have been genetically modified to redirect their antigenic specificity against malignant cells. The power of this approach is made clear by the remarkable success that CAR T cells, specific for the B-cell molecule CD19, have shown in inducing durable remission times in human patients with relapsed, refractory B-cell malignancies. Recognition of this success came last year when the FDA approved the use of CD19-targeted CAR T-cell therapy for ALL in children and young adults.

In CAR T-cell therapy, T cells are collected from the patient’s blood and genetically modified in the laboratory to express a protein receptor (CAR) on
CHALLENGES WITH CAR T-CELL THERAPY

Dr. Mason described several challenges associated with CAR T-cell therapy. Although it has shown substantial clinical benefit in humans with hematologic malignancies, CAR T-cell-based therapy still faces hurdles when directed against solid tumors. Not only is it challenging to generate these products from patients with advanced neoplastic disease because of the presence of immunosuppressive factors and intrinsic T-cell signaling defects, but it is also difficult to get these genetically redirected T cells to penetrate the solid tumor and function optimally in the immunosuppressive tumor microenvironment.

“CAR T-cell therapy is extremely potent, and it can cause significant morbidity when adoptively transferred cells are fully activated,” Dr. Mason emphasized, explaining that life-threatening cytokine release has been reported in some human patients. Massive cytokine release resulting from immune activation can manifest in various ways, ranging from fever to organ dysfunction to disseminated intravascular coagulation and death. Neurotoxicity is another concerning adverse effect that has been seen in some human patients; however, the seizures that have been reported with CAR T-cell therapy can be managed medically and appear to be transient.

Dr. Mason also stressed the need to overcome adaptive resistance to CAR T-cell therapy. For example, some patients with CD19-positive B-cell leukemia who are treated with CD19-targeting CAR T cells may relapse with CD19-negative B-cell leukemia. This is because immune pressure leads to the emergence of leukemic cells that have spliced out the epitope that is recognized by the CAR T cells. This leads to patient relapse with an apparent CD19-negative leukemia.

CAR T-CELL THERAPY IN DOGS

“Canine patients represent a parallel system to humans in which we can develop and evaluate next-generation CAR T-cell therapy,” Dr. Mason said. The progression of canine cancers more closely parallels that of human cancers than is seen in animal models of induced cancer. In particular, the biology, behavior, and genetics of some spontaneously occurring canine cancers are comparable to the characteristics of those that occur in humans. Dr. Mason’s laboratory has adapted CAR T-cell technology for use in dogs. This serves 2 purposes: to provide a model system to evaluate next-generation CAR T-cell therapies and to provide a novel and hopefully more effective therapeutic approach to providing durable remissions and cures in canine patients with B-cell malignancies.

To evaluate next-generation CAR T-cell therapies in dogs, Dr. Mason stressed the need for methods to effectively expand and genetically modify canine T cells for adoptive transfer. Her laboratory has developed an in vitro system for canine T-cell expansion. This system is based on K562 cells, a human erythroleukemic cell line that has been stably transduced to express the canine costimulatory molecules that are needed to support T-cell activation.

She and her team tested the system on peripheral blood lymphocytes isolated from healthy dogs. In the absence of exogenous cytokines, this method produced a 50-fold expansion of T cells. In contrast, adding exogenous cytokines to the system dramatically enhanced T-cell proliferation, leading to a 250-fold expansion.

After collecting peripheral blood from dogs with lymphoma, the investigators used this system to expand the patients’ white blood cells in vitro and were able to produce sufficient canine T cells to perform CAR T-cell infusions.

Results from early studies have indicated that CAR T-cell therapy has an effect in canine patients with B-cell malignancies.

In collaboration with investigators at The University of Texas MD Anderson Cancer Center in Houston, Dr. Mason’s laboratory developed a CD20-targeting, second-generation CAR, and they are evaluating its ability to eliminate CD20-positive B cells in dogs with B-cell leukemia and B-cell lymphoma.

According to Dr. Mason, results from early studies have indicated that CAR T-cell therapy has an effect in canine patients with B-cell malignancies. It has led to stable disease in these patients for a period of time, reversal of the ratio of B cells to T cells in the lymph nodes, and an increase in the number of cytotoxic CD8 T cells in peripheral blood as well as clear evidence of immunologic pressure against CD20. Currently, however, the therapeutic effect is transient.

Dr. Mason acknowledged that investigators have experienced problems generating CAR T cells from human and canine patients with advanced disease and discussed potential strategies to help overcome challenges. “To deal with this, we have to optimize T-cell production strategies,” she said. She also stressed the need to consider moving away from using an autologous CAR T-cell product to using a universal CAR T-cell product. “These products will obviously require further genetic modification to eliminate the T-cell receptor and major histocompatibility complex molecules to prevent graft-versus-host disease and universal CAR T-cell rejection, respectively,” she explained.

Antigen escape leading to CAR T-cell resistance is another problem to overcome in both humans and dogs, Dr. Mason noted, suggesting that adopting a dual CAR targeting approach against CD19 and CD20 would be a rational strategy to reduce adaptive resistance.

“So far, we have not seen significant adverse effects using canine CAR T cells in vivo,” she explained. “We have not appreciated any cytokine storms or neurotoxicity.” However, Dr. Mason believes that as the technology improves in dogs, some of these adverse effects will inevitably emerge. This is because as the number of CAR T cells administered increases to achieve more durable effects, it is likely that more cytokines will be produced, and these cytokines mediate the adverse effects.

Nevertheless, the stage is set for CAR T cells to enter the veterinary oncology arena, and there are high hopes that this may lead to the durable remission in canine patients with B-cell lymphoma that has so long eluded us.
Advances in Feline Heart Disease Diagnosis
Combining radiology, echocardiography, and cardiac stress marker results can bring clarity to ambiguous cases.

By Natalie Stilwell, DVM, MS, PhD

In Columbus, Ohio, Dr. Stepien presented the latest tools for diagnosis of cardiac abnormalities in cats. She began by emphasizing the importance of differentiating heart disease and heart failure in the feline patient.

Differentiating Heart Disease and Heart Failure
Cardiac disease, she said, is typically monitored rather than clinically treated in cats, whereas cardiac failure is almost always treated. Heart disease is defined as a physical or functional abnormality of one or more components of the cardiovascular system; heart failure occurs when cardiac output provides inadequate blood pressure for organ perfusion despite normal hydration status. Cardiac failure may manifest clinically as hypotension due to low cardiac output or as congestion, edema, or other fluid accumulation due to sodium and/or water retention.

Detecting asymptomatic heart disease in cats is not as straightforward as in dogs. Dr. Stepien estimated that approximately one-quarter to one-third of overactive or healthy cats have heart murmurs. About half of cats with murmurs have diagnosable cardiac disease, while in the other half the murmurs are innocent. Dr. Stepien emphasized, “No murmur likely means no disease.” She added that the most common life stage for development of myocardial disease begins at about 6 to 8 years of age and decreases after 12 to 14 years.

Gallop Rhythm and Cardiac Arrhythmia
To determine whether a heart murmur is causing disease, Dr. Stepien advised examining for additional abnormal findings, especially a gallop heart sound or cardiac arrhythmia. Gallop heart sounds occur when rapid ventricular filling suddenly stops because of abnormal stiffness of the ventricular wall, thus generating a third heart sound. The condition, which may be temporary or permanent, can be caused by a variety of pathologies, including hypertrophic or dilated cardiomyopathy, ventricular fibrillation (especially restrictive cardiomyopathy), and neoplasia. In particular, Dr. Stepien noted, feline lymphoma can infiltrate and stiffen the heart wall. Increased ventricular dilation leading to gallop heart sounds can also occur in patients with renal disease after receiving fluid therapy because of overhydration and increased blood volume. The combination of a cardiac murmur and an arrhythmia also increases the likelihood of true cardiac disease, she said.

Heart Murmur in a Healthy Cat: Should I Still Worry?
A heart murmur may warrant additional investigation even in patients with no outward clinical signs, Dr. Stepien noted. Further diagnostics should be performed before any cat with a murmur undergoes anesthesia or receives fluid therapy. Also, certain systemic diseases, such as occult hypertension, anemia, and hyperthyroidism, can exacerbate a murmur and should be ruled out. Finally, some clients may encourage further diagnostics for peace of mind.

Diagnostic Imaging for Cardiac Abnormalities
Dr. Stepien noted that radiology is more useful than echocardiography for assessing congestive heart failure, but echocardiography is needed to evaluate cardiac anatomy. Many cats with cardiac disease lack significant atrial and/or ventricular enlargement when imaged by echocardiography. Obese cats frequently deposit fat in the pericardium, thus enlarging the cardiac silhouette on radiography even in the absence of cardiac disease. In such cases, Dr. Stepien advised examining the pulmonary vessels as an additional indicator of cardiac disease. She also noted that if the heart touches the diaphragm, it is likely enlarged.

Another limitation of radiography is the large overlap in vertebral heart scores between normal and abnormal cats. According to 1 study, a vertebral heart score of 8 or higher is only 78% sensitive for detecting left heart disease with no or mild left atrial enlargement; however, sensitivity increases to 91% if left atrial enlargement is mild to moderate. Study results showed that vertebral heart score was 82% specific for detecting left heart disease, regardless of left atrial size. Therefore, vertebral heart score may be an unreliable predictor of cardiac disease.

Echocardiography holds particular value for screening at-risk cat breeds, including the sphynx and Maine coon, for hypertrophic cardiomyopathy before breeding. As noted earlier, diagnostics such as echocardiography should be performed before administering anesthesia or fluid therapy in patients with heart murmurs. Echocardiography is also the most effective tool for detecting intracardiac thrombi.

Dr. Stepien noted that thoracic ultrasound is much less stressful than radiographs to perform on an unstable patient, and even a brief or limited scan can still provide valuable information, such as the presence or absence of pleural effusion. She allows particularly fragile patients to remain sternal and receive supplemental oxygen rather than placing them in lateral recumbency. Dr. Stepien emphasized looking at the left atrium, which will likely be enlarged in a cat with signs of congestive heart failure, such as pleural effusion and pulmonary edema. A left atrium measuring more than 1.5 times the diameter of the aorta likely indicates heart disease.

(continued on page 18)
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Thoracic ultrasound can also detect the presence of lung infiltrates related to heart disease, as in cases of pulmonary edema. The dorsal lung field offers an ideal location to view lung tissue by orienting the ultrasound probe between the ribs. Although the appearance of white horizontal lines, or A lines, is normal on thoracic sonography, fluid in the lungs will cause white vertical lines or “rockets” that descend vertically from the probe location.

Although echocardiography remains the gold standard for diagnosing heart disease in cats, Dr. Stepien acknowledged that many veterinarians lack access to this tool. “That doesn’t keep you from being a good practitioner,” she assured the audience. Recent advancements in cardiology include measurement of cardiac stress markers, she said.

**BNP MEASUREMENT**

B-type natriuretic peptide (BNP) is a hormone that regulates blood pressure and fluid balance through renal sodium and water loss as well as vasodilation. BNP is synthesized and stored in the cardiac myocytes as the promolecule proBNP. Secretion of proBNP by the myocytes is continuous and increases with excessive stretching, pressure, or expansion of the cells. Because many forms of heart disease, such as hypertrophic cardiomyopathy, cause excessive stretching of the heart muscle, BNP is an appropriate marker for assessing for the presence of heart disease. In general, the amount of circulating BNP correlates with severity of cardiac stress.

**ELISA and SNAP Tests**

In veterinary medicine, quantitative and semiquantitative tests are available to estimate plasma N-terminal (NT)-proBNP concentrations. The measured form of BNP, NT-proBNP, is 1 cleaved end of the secreted proBNP molecule. NT-proBNP is stable and has a long half-life, making it a good indicator of circulating BNP concentrations.

The enzyme-linked immunosorbent assay (ELISA) NT-proBNP test is available from Idexx as the feline CardioPet proBNP test, which provides a quantitative result, as the amount of visible marker is proportional to the amount of circulating BNP. The SNAP feline semiquantitative test provides a positive or negative result for NT-proBNP, with a cutoff value of about 150 pmol/L. A “very dark” positive dot indicates a relatively high value, suggesting more severe cardiac stress.

**Interpreting High BNP Concentrations**

Heart disease and heart failure both raise NT-proBNP levels; however, increased NT-proBNP may occur in patients with “normal” echocardiogram findings. In such cases, it is important to rule out other causes of increased NT-proBNP. Several diseases, including systemic hypertension and hyperthyroidism, may increase NT-proBNP by affecting blood volume or cardiac work–related stress. Concentrations may also rise in cats with true renal insufficiency or prerenal azotemia due to dehydration, as NT-proBNP excretion occurs in the kidneys. Dr. Stepien noted that renal disease appears to have a lesser effect on NT-proBNP concentration in cats than in dogs and humans.

As a general rule, the greater the NT-proBNP concentration, the more severe the abnormality is. Primary cardiomyopathy causes higher NT-proBNP concentrations compared with secondary cardiomyopathy due to hyperthyroidism or hypertension. Heart disease cases also have higher NT-proBNP values than cases of impaired NT-proBNP excretion due to renal disease. Dr. Stepien added that congestive heart failure usually corresponds to higher NT-proBNP values than does heart disease alone. She provided general guidelines for interpreting NT-proBNP SNAP results (Box).

Although the exact cutoff values are not clear, 1 study determined that a quantitative NT-proBNP test result of 99 pmol/L or higher effectively detected subclinical cardiomyopathy (sensitivity 71%, specificity 100%). Results from another study showed that dyspneic cats with a plasma NT-proBNP value above 265 pmol/L were likely to have heart failure (sensitivity 90%, specificity 88%). Cats with congestive heart failure had a median NT-proBNP value of 754 pmol/L, and 90% of values exceeded 300 pmol/L. A higher NT-proBNP value, Dr. Stepien stated, should increase confidence in a congestive heart failure diagnosis.

Quantitative NT-proBNP measurement using ELISA can also help clarify ambiguous situations, such as differentiating innocent murmurs from associated disease or correlating respiratory signs with heart failure. NT-proBNP assessment, however, does have limitations. The test cannot specify the type of heart disease present, nor will it provide an indication for therapy. Also, research has not yet established whether NT-proBNP measurement can reliably detect preclinical genetic disease. The value of NT-proBNP measurement, Dr. Stepien stressed, lies in aiding interpretation of other clinical findings.

**Which Test Should I Choose?**

Clinical applications differ for the semiquantitative SNAP and quantitative ELISA tests, Dr. Stepien stated. The SNAP test is best used when the extent of cardiac stress needs to be determined immediately, as the quantitative test costs more and has a 12- to 24-hour turnaround time. The SNAP test is also particularly valuable for confirming suspect-normal cases, particularly before administering anesthesia or fluid therapy. Examples include a relatively low-risk, young cat with a murmur or a dyspneic cat with a history of respiratory disease but no history of cardiac disease.

Dr. Stepien reminded the audience that the cutoff value of 150 pmol/L NT-proBNP for the SNAP test is similar to the approximately 100 pmol/L cutoff for asymptomatic heart disease. Therefore, a positive SNAP test likely indicates the presence of heart disease, whether subclinical or clinical.

Dr. Stepien recommended the quantitative ELISA test for suspect heart disease cases for which an echocardiogram cannot be performed, as the quantitative test still provides an indication of disease severity. The quantitative test can also help track heart disease cases over time as well as provide further clarity after a positive SNAP test result.

**My Patient Has Elevated BNP Levels. Should I Treat for Cardiac Disease?**

Dr. Stepien reminded the audience that a positive SNAP or ELISA NT-proBNP test result should always be interpreted in combination with physical examination and other diagnostic findings. “This way,” she said, “one can look for suggestive evidence of heart failure, such as auscultatory or radiographic abnormalities, arrhythmia, and dyspnea.” Treatment should be initiated if clinical signs indicate cardiac failure.

**Caveats of Measuring NT-proBNP**

No diagnostic test is perfect, and the NT-proBNP test has limitations. The test is more sensitive than echocardiography; therefore, NT-proBNP levels may rise before abnormalities are visible on an echocardiogram. Likewise, marginal increases in NT-proBNP may occur because of other diseases or may hover close to the cutoff point for abnormality. Finally, a patient’s NT-proBNP values can vary as much as 13% day to day and 21% week to week.

In summary, the NT-proBNP test is particularly helpful for cases in which ruling out heart disease helps avoid more costly evaluation or for those in which physical examination and diagnostic tests have provided inconclusive evidence of heart disease.

**CLOSING REMARKS**

Evaluation of feline cardiovascular disease should include a combination of available diagnostic tools, including physical examination, thoracic radiography, electrocardiography (in cases of arrhythmia), echocardiography, and NT-proBNP measurement. Diseases with secondary cardiac effects, such as hyperthyroidism and renal disease, should also be considered in cats with cardiac abnormalities.
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Current Options for Managing Canine Osteoarthritis

A host of effective modalities are available for alleviating discomfort and improving mobility in dogs with degenerative joint disease.

(continued from front cover)

But this vicious circle can be broken with the help of several existing and new treatment modalities. American Veterinarian® spoke with Dr. Dycus about today’s best practices for managing OA.

What is your overall approach to the patient with OA?
David Dycus, DVM, MS, CCRP, DACVS-SA: In people with OA, most of the stiffness, soreness, and pain come from the loss of range of motion, and I think the same probably applies to dogs. If we can maintain as much range of motion as possible and exercise them daily, they’re going to have less stiffness and more comfort.

It used to be that we prescribed an anti-inflammatory and there wasn’t much more we would do. What has emerged in the past decade or so is the concept of multimodal management, the idea that anti-inflammatories can be combined with other modalities to better manage the condition.

We have to come at OA from every angle, with the ultimate goal of maintaining comfort and daily exercise for the dog. Owners don’t want to think they are hurting their pets, so it’s our job to ensure they stay comfortable and exercise to maintain range of motion and ideally minimize or slow disease progression as best as possible. And exercise doesn’t mean going into the backyard and chasing squirrels. It means getting outside and going on walks. Ideally, most dogs should be able to go comfortably on at least two 20-minute leash walks on flat ground every day. Once they can achieve this, then the sky is the limit in terms of time, distance, terrain, and elevation.

To achieve that level of comfort, we combine various modalities, typically starting with pain management.

EVALUATING AND MANAGING PAIN
How do you manage their pain?
Just as in people, dogs with OA have periods of relative calmness and then periods of flare-ups during which clinical signs are acutely exacerbated. It is during the periods of calmness where we have our “baseline [management] approach.” This includes joint supplements such as glucosamine, chondroitin, and omega-3 fatty acids. However, the most important aspect of the baseline approach is daily exercise and maintenance of a lean body weight. If a patient with OA deviates from its baseline, this can indicate a flare-up. When this happens, we take a step back and ask ourselves what we can do to get the flare-up under control so that the patient can return to its baseline. During a flare-up there is more pain and discomfort, so step 1 is getting this under control.

We may start with pharmaceuticals such as nonsteroidal anti-inflammatory drugs (NSAIDs), but the goal is to use these at the lowest dose and as infrequently possible. This means using an NSAID for 10 to 14 days during the early phases of OA knowing that at some point in the future the patient may need daily NSAID...
support. As a profession, we’ve got to move away from offering only an anti-inflammatory and an opioid and thinking there is nothing more we can do.

Other pharmaceuticals that can be considered are opioids such as codeine. However, it should be remembered that opioids are not designed for chronic use. Gabapentin, amantadine, and amitriptyline, among others, can be considered along with an NSAID.

Do you prescribe tramadol for pain management?
I’ve moved away from tramadol for joint pain. I think there has always been controversy over tramadol’s effectiveness, with no real clinical evidence that it was helpful, and there seems to be a consensus now that it doesn’t work very well to control joint pain. One recent study used both positive and negative controls (placebo) and found that there was no improvement in peak vertical force or vertical impulse in dogs on tramadol versus placebo. Rather than it being a true opioid and controlling pain, I think tramadol likely affects serotonin levels. So the patient may be a bit spaced-out, but they are probably still painful.

Is grapiprant effective?
Grapiprant (Galliprant; Elanco) is a prostaglandin-receptor antagonist that targets the EP4 receptor that’s involved in OA-associated pain and inflammation. Formulated only for dogs, grapiprant can help animals that haven’t tolerated or responded to traditional NSAIDs. It’s also associated with fewer hepatic, renal, and gastrointestinal side effects. It might be a good go-to for some of those older patients who are stuck between a rock and a hard spot because they can’t tolerate traditional anti-inflammatories.

In what other ways can pain be kept under control?
There are a lot of avenues beyond pharmaceuticals to make these patients comfortable. Other disease-modifying OA agents, such as joint supplements with glucosamine, chondroitin, omega-3 fatty acids, and polysulfated glycosaminoglycans, can be incorporated, for example.

Adding to our multimodal management approach during a flare-up is the incorporation of formal physical rehabilitation and intra-articular injections. Physical rehabilitation can be used to allow active muscle contractions while minimizing the stress being placed on the joints. In this situation we can allow a patient to remain active and thus maintain range of motion while simultaneously working to help get pain under control. Rehabilitation therapies are a great nonpharmaceutical avenue for managing pain and in many cases can help us lower the dose or frequency of pharmaceuticals.

Intra-articular injections include a variety of substances, such as steroids, hyaluronic acid, or regenerative medicine (platelet-rich plasma [PRP] and/or mesenchymal stem cells). Intra-articular injections are a way to further reduce the inflammatory response in a more target-directed way over the oral analgesics. These products can achieve a high concentration directly at the joint.

We must always be evolving and taking a multimodal, patient-centered approach rather than a cookbook approach.

Once they’re comfortable we get them back to their baseline. It’s important to remember that what works during one flare-up may not work for the next. We must always be evolving and taking a multimodal, patient-centered approach rather than a cookbook approach.

REHABILITATION THERAPY
How do you incorporate rehabilitation into the treatment plan?
Manual therapies like stretching and range-of-motion exercises can help during the initial phases of rehabilitation when patients are still painful. In addition, we can add in cryotherapy and warm packing during various situations to further help with our manual therapies.

In addition to manual therapies, therapeutic exercises can be used initially to help with balance and proprioception. These exercises can include wobble boards, peanut balls, and balance balls. Once the patient is comfortable we can use therapeutic exercises to increase muscle strength and improve endurance. This can be accomplished with things such as caullietta poles, sit-to-stand exercises, dancing exercises, and many others.

Therapeutic modalities such as electrical stimulation, shockwave, and laser therapy can help minimize inflammation, alter blood flow, and assist in tissue healing as well as help resolve some of the compensatory issues that develop when a patient is not loading a joint properly. We can also use therapeutic ultrasound to warm tissues or to facilitate stretching and help with extensibility and distensibility of some of those soft tissues to reorient collagen fibrils as well as help with periarticular fibrosis.

The underwater treadmill is great because higher water levels take the load of stress off the joint. If we take the water level up to the level of the greater trochanter in a 100-lb dog, for example, that dog is going to feel as if he weighs 38 lb. So, he can walk at a normal pace, starting out for about 7 to 10 minutes, and all that stress is off the joint but the dog still has to actively contract the muscles.

Once the pain is under control, we can start to lower the water level to make the exercise more challenging. This will help build muscle as well as help with maintaining range of joint motion and continuing to improve cardiovascular health and endurance.

How similar is rehabilitation in human and veterinary medicine?
Much of what we know in veterinary rehabilitation has been derived from human rehabilitation. When people go for physical therapy, they do exercises at the facility and are then given “homework” to build on what they’ve started. That way, when they come back to the facility they can continue to advance.

We do the same thing in veterinary medicine. We’ll have formal rehabilitation sessions once or twice a week with a skilled therapist, and we’ll also assign a home exercise plan. I tell owners there are 2 parts to the rehab plan: the part where you come in and your pet undergoes formal sessions, and then every day you’ll have homework so that when your dog comes back we’ll be able to advance our rehabilitation plan.

The nuts and bolts of physical rehabilitation is the home exercise plan, and core to that plan is walking, walking, walking. Once the pet gets further along in terms of improvement and comfort we can start to add in uneven terrain, inclines and declines, and stairs, depending on what we’re trying to achieve.

REGenerative medicine
Can you talk a bit about regenerative medicine in OA? What is it exactly?
Regenerative medicine is a broad interdisciplinary field that includes any type of biologic that is focused on the repair, replacement, and/or regeneration of tissues. The overall goal is reduced pain and inflammation and improved healing of injured tissues. Regenerative medicine in OA commonly includes PRP or the combination of stem cells and PRP.

There’s a lot we know about regenerative medicine and there is even more we don’t know. The biggest misconception is that people think we are generating new tissue or growing new cartilage, and that is definitely not the case. We’re not taking a 12-year-old dog with end-stage elbow OA and injecting stem cells or PRP and all of a sudden growing new cartilage. What we are doing is taking a very high concentration of growth factors and anti-inflammatory agents to an area of relatively poor tissue healing with the hope that we can achieve a reduction in the inflammatory response.

Where do stem cells and PRP come from?
For PRP, we gather a blood sample that is processed through a machine that renders a solution with a higher concentration of platelets and eliminates red blood cells and certain white blood cells. Within
the platelets are alpha granules that contain a rich source of growth factors and anti-inflammatory mediators. Think about when you cut yourself. A clot forms at the wound and within that clot the platelets contain these alpha granules that release various growth factors as well as cytokines. These cytokines are able to recruit reparative cells to the area of injured tissue. The clot also provides a scaffolding to which cells attach to facilitate repair. We are using PRP in a similar function.

Stem cells are typically harvested from the patient’s own fat or bone marrow. The tissue can either be sent to a lab for the stem cells to be isolated and cultured, or the tissue can be processed in-house. It should be noted that stem cells that are isolated should have unique characteristics that should be identified and characterized by the lab processing the cells; this will create a homogenous population of stem cells. Tissue that is processed in-house creates what is called either the stromal vascular fraction (SVF) for fat or bone marrow aspirate concentrate (BMAC) that is a heterogeneous population of cells with the thought that some portion of the SVF/BMAC contains stem cells but the actual amount of stem cells is unknown. Stem cells primarily provide trophic support in helping diminish tissue injury, promote neovascularization, inhibit fibrosis, and help recruit resident cells in the region for tissue repair. When stem cells are used with PRP, the PRP creates a scaffolding for the cells to attach to, which in theory may have a more beneficial effect than using either alone.

What type of research has been done with regenerative medicine?
When any new concept is introduced to patients, whether humans or animals, our first mandate is to do no harm. When used appropriately, both PRP and stem cells have been shown to be safe with minimal to no adverse effects. In addition to safety, we also need to have faith in the systems used for processing to ensure that we are delivering to our patients what we think we are to achieve this, the systems need to be validated. However, we should use caution when using the word “validated” because there are so many factors between and within patients that can alter platelet and stem cell function, number, and collection. In addition, different collection and processing methods can have an effect on what is produced. Current work has been completed with PRP to show that the machines used for processing can provide repeatable results. To date, there is no published information on in-house processing of SVF/BMAC. Again, between- and within-patient variables will make this challenging if not impossible to standardize.

Once the systems are noted to be repeatable, then we need to determine what we want in a product and what dose and how often it needs to be given, and we need to prove efficacy through multicentered blinded placebo-controlled studies with objective outcome measures and appropriate statistical power to detect differences.

What’s interesting is that many of the translational studies using regenerative medicine for human application come from animal models, often using dogs. The challenge is that many of these studies are published in human journals; they’re not going to show up in our veterinary literature, so we won’t necessarily know about them. Nevertheless, extreme caution should be used when evaluating these studies as controlled tissue injuries don’t always match spontaneous injuries that are seen clinically. Also, although stem cells among species are similar there are some key differences. This highlights the need for caution that definitive conclusions about canine stem cell differentiation based on literature from other species is not made regardless of the tissue source.

What is your advice to veterinarians about regenerative medicine?
Pet owners are asking about some of these minimally invasive, nonpharmacologic approaches to OA management, and we need to be prepared to give them appropriate information and realistic expectations. Some people are jumping in headfirst, but we’re really just getting our toes wet with regenerative therapies in veterinary medicine and there are a number of things we need to evaluate to determine how to use these therapies appropriately. With OA, for example, depending on the level of changes present, the patient may require a certain type of PRP or stem cell therapy. Should every product be used in the same way, or do we take more of a patient-centered approach? How many injections do we give, and how frequently? When do we use PRP or stem cells alone, and when do we combine them? There is a lot of work yet to be done to determine how we can best use regenerative therapies to improve patient care, but I think it’s a promising technology that’s showing some benefits when used in the appropriate manner.

OTHER NEW THERAPIES
What other types of treatment are on the horizon?
I think in the future there will be a move toward more molecular-driven therapies rather than giving a medication to block an entire pathway. We have seen the beginnings of this in veterinary medicine with the development of a monoclonal antibody therapy directed toward nerve growth factor. In people, nerve growth factor has been shown to be a significant source of pain and inflammation associated with OA. Results of clinical trials have shown relief of OA pain for about 4 weeks in dogs and 7 days in cats. This was originally developed by a company called Nexvet Biopharma, which was acquired by Zoetis. Since the acquisition by Zoetis we have not heard any more about this promising technology.

I’m also working on a clinical trial for the use of a targeted pulsed-electromagnetic field (PEMF) therapy for OA management.

What is that?
Targeted PEMF therapy, which has been FDA approved for use in people, delivers a targeted pulse of electric current to tissue. Initially, many companies thought that a powerful magnet was needed or that “more is better,” which we now know is not the case. We’ve known since the 1970s that low-powered PEMF can help with bone healing as well as reducing inflammation. While the exact mechanisms of action are unknown, the major thought is the binding of calcium and calcimodulin by the PEMF, which naturally initiates an anti-inflammatory cascade. This is accomplished by leading to the production of nitric oxide, which is a principal anti-inflammatory molecule that assists in reducing pain, improving blood flow, and reducing edema. This was a blinded placebo-controlled pilot study using objective outcome measures. We are still awaiting the initial results to determine whether a difference was noted.

References available at AmericanVeterinarian.com.
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Photobiomodulation can improve healing—and quality of life—for veterinary patients with a host of health conditions.

By David S. Bradley, DVM, FASLMS

It is estimated that about 40% of veterinary practices offer laser therapy, officially termed photobiomodulation (PBM), as part of their armamentarium. This is due in large part to a greater understanding of laser therapy and a maturing of the technology, making it safer, easier to use, and more effective on for a wider variety of clinical conditions.

HOW LASER THERAPY WORKS

Laser therapy uses a wavelength-specific form of PBM to restore normal biological function and repair injured or stressed cells. Cellular chromophores within the bloodstream and tissue mitochondria absorb the laser energy, stimulating or enhancing a series of primary biochemical processes, along with a broad cascade of secondary and tertiary effects.

The primary response is a direct photochemical reaction similar to photosynthesis or vitamin D production in the skin. This occurs when photons in the infrared range emitted by the laser reach the cell mitochondria and membranes. The photonic energy is converted to chemical kinetic energy within the cell, resulting in improved efficiency of the respiratory chain within the cell mitochondria due to changes in membrane permeability, nitric oxide formation, increased oxidative metabolism to produce more adenosine triphosphate (ATP), and improved signaling between mitochondria, nuclei, and cytosol.1 Other direct effects include the production of reactive oxygen species such as superoxide dismutase and a beneficial shift in the redox state.

Secondary and tertiary reactions amplify the primary photochemical reactions, resulting in improved cell metabolism and regulation of signaling pathways responsible for tissue repair. Blood vessels and lymphatics respond favorably, enhancing tissue perfusion and providing oxygen and nutrients needed for recovery.2 Studies document enhanced cell migration, RNA and DNA synthesis, cell mitosis, protein secretion, and cell proliferation.2 This enhances healing and production of collagen and epithelial cells.

PBM also stimulates a more normal distribution of type I and type III collagen during the healing process.3,4 Damaged muscle and nerve cells heal faster and/or function better. The immune system, including white blood cells, functions efficiently to fight infection and clean up debris.

Not only does laser therapy enhance positive cellular processes, but it inhibits negative processes such as pain, exuberant inflammation, and aberrant immune responses. In vivo, it also stops further growth when healing is complete. This acceleration of normal healing and tissue regeneration without producing overgrowth or neoplastic transformation is a critical and unique feature of laser therapy.2,11

THERAPEUTIC USES IN VETERINARY MEDICINE

Laser therapy offers 3 main benefits: analgesia, reduced inflammation, and faster and better recovery. It allows veterinarians to improve and resolve conditions that traditionally have been less responsive to other therapies. Soft tissue, musculoskeletal, neurologic, dermatologic, and even some intra-abdominal and intrathoracic conditions can be improved or managed more efficiently and with fewer drugs by adding laser therapy to the treatment regimen.

According to the investigators in a University of Florida study on laser therapy in spinal cord-injured dogs, “the results were so profound that we’re doing this procedure now on all dogs that come to us with this condition.”12 Other areas of interest include peripheral nerve injury, traumatic brain injury, stroke, and even depression.

Laser therapy is used in a wide range of dermatologic conditions, from acute injuries, trauma, and postoperative applications to management of chronic allergic and autoimmune/idiopathic syndromes including otitis, perianal fistulas, lick granulomas, and hot spots.

Many pathologic lung conditions respond favorably to laser therapy.13-15 It has helped slow the progression and/or decrease the intensity of drug therapy in conditions such as interstitial pulmonary fibrosis (Westie lung disease), feline asthma, and even tuberculosis.

Patients with chronic kidney disease have shown clinical improvement related to appetite, well-being, and nausea. The addition of laser therapy has also demonstrated improvement in chronic bladder issues including persistent infections and feline idiopathic cystitis, and it has been used as an adjunct to improve inflammatory bowel syndromes and other enteropathies.16 There are even anecdotal reports of decreased morbidity and mortality in parvovirus enteritis with the addition of laser therapy.

WHAT TO CONSIDER

To capitalize on laser therapy, veterinarians must understand the optimal parameters that allow it to be so effective across such a broad range of applications. The most important features to consider when buying
Laser therapy can be used to treat cervical intervertebral disk disease (left) or as an adjunct for periodontal disease treatment (above).

References available at AmericanVeterinarian.com.

Dr. Bradley is the veterinary medical director for K-LASER USA in Franklin, Tennessee. He began using lasers in private practice in 1999 and has worked with all types of surgical and therapeutic lasers. He was granted Fellow status in the American Society of Laser Medicine and Surgery. He has authored numerous articles and chapters and has lectured nationally and internationally on veterinary laser use.

a laser are power, wavelength, delivery mode, and training and support. Buying a laser with the widest array of options or adjustability will deliver the best clinical results on the broadest number of patients and conditions.

**Power**

Power (watts) times time (seconds) delivers the dose (joules). In laser therapy, joules/cm² is as critical to laser success as mg/kg of an antibiotic or mL/kg of fluid is to clinical success. The power should be adjustable from low, for small or superficial conditions or patients and acupuncture points, to high, to efficiently deliver enough energy (joules) to saturate/stimulate acupuncture points, to high, to efficiently deliver enough energy (joules) to saturate/stimulate large areas or patients as well as deep-seated and/or chronic musculoskeletal conditions.

**Wavelength**

The availability and selection of wavelength are important for optimal stimulation of different chromophores as well as levels of penetration. Roughly, this corresponds to wavelengths between 600 and 1100 nm. Shorter wavelengths are absorbed more superficially and thus cannot penetrate as readily as longer wavelengths. Wavelengths in the visible red range (600 nm) are highly absorbed by melanin and other superficial receptors. These can enhance wound healing. They may also stimulate trigger points and acupuncture points and cause release of secondary messengers that may improve other deep-seated conditions. Absorption spectra data have shown that wavelengths near the 970-nm range have moderate increased absorption by water.¹⁷,¹⁸ This is the least penetrating infrared wavelength. With higher-powered lasers, this can create some thermal gradients and increase circulation. The 905-nm wavelength is nearest the peak of the hemoglobin absorption curve. This can enhance oxygen release more efficiently. Results from recent studies have indicated that this wavelength may be able to increase oxygen release even more efficiently to tissue over the 970- to 980-nm wavelengths.

Wavelengths nearer the 800-nm range (750-830 nm) are at the peak of absorption for the cytochrome c oxidase enzyme. This is the rate-limiting step in the conversion of oxygen to ATP within the electron transport cycle. These wavelengths will accelerate the production of ATP within the mitochondria. There is new interest in the 1064-nm wavelength, particularly for its photochemical effects. This wavelength is farthest from the point of maximum melanin production, has a relative trough in the water absorption spectrum, and is still at the upper level of the cytochrome c oxidase absorption band. Therefore, it has very good penetration depth along with potent biostimulatory abilities. Having all 4 (or 5) wavelengths as well as the ability to use any combination will offer a synergistic effect and/or a wider range of treatment options across a broader spectrum of clinical conditions and patients.

**Delivery Mode**

Delivery mode (continuous wave, pulsed or modulated, superpulse) will enhance overall improvement and produce better clinical results. Varying pulse rates enhance different physiologic responses as well as different tissue types to a greater degree.¹⁹,²¹ Optimal pulsing frequencies are still being studied, but current literature consistently shows that overall clinical results will be higher if pulsing phases, rather than continuous-wave delivery, are part of the treatment protocol.²²

**Training**

Although the technology behind laser therapy may sound complicated, training is paramount and the learning curve is not high. Ignoring or dismissing certain features will decrease the consistency in results, the degree or quality of improvement, and the number of conditions that will respond favorably. Today’s lasers are very safe and user-friendly. The protocols already set up in advanced therapeutic lasers incorporate all the parameters in a “point-and-shoot” instrument. This ease of use, along with proper training, will allow veterinary practices to institute laser therapy quickly and easily. It can and should be delegated to the staff for the most efficient treatment and economic benefits.

**CONCLUSION**

Future studies will enhance our knowledge of the variety of applications and the optimal parameters for the most effective laser therapy. The goal is not to just make our patients more comfortable—we want to return them to their normal activity level, restore range of motion, and improve muscle strength and function. Laser therapy allows performance animals to recover more quickly and more fully to regain their competitive edge and helps pets remain active members of the family.
Vision in Dogs and Cats

Do animals see in black and white? Answers to common questions from clients.

By Ron Ofri, DVM, PhD, DECVO

(continued from front cover)

DO YOUR PATIENTS SEE IN BLACK AND WHITE?

We’ll start with the most popular question: Are cats and dogs able to see color? Cone photoreceptors are responsible for color vision in all species. The richness of color vision, and the number of shades that an eye can see, are determined by the number of cone photopigment populations and the degree of overlap in their absorbance spectrum.  

To better understand how your patients see, it’s helpful to know that humans have 3 cone photopigment populations, with peak absorbance in the red, blue, and green wavelengths—which is why these are our 3 primary colors—making humans a trichromatic species. On the other end of the spectrum are monochromatic species, which have only a single photopigment population. This type of vision is characteristic of nocturnal species, which can perceive only shades of a single photopigment, usually with a red/green hue.

Most domestic animals are dichromatic, meaning they possess 2 photopigment populations. So, contrary to popular belief, domestic animals do not see in black and white. They have color vision, although not as rich as that of us trichromatic humans.

Cats, dogs, cattle, and horses all have 2 photopigment populations, with absorbance peaks of about 440 and 555 nm. Consequently, these species can see blue but have difficulty distinguishing between red, green, and yellow. Color vision in these species is analogous to that of “color-blind” humans, who are usually missing their red and green cone population (Figure 1).

If you think humans have the most superior vision, however, you’d be mistaken. Many fish and bird species are tetrachromatic, meaning they have a fourth photopigment absorbing light in the ultraviolet end of the color spectrum. As such, they possess color vision that is significantly richer than humans.

VISUAL FIELDS

The frontal part of the visual field is covered by both eyes, resulting in binocular vision, which is traditionally required for depth perception. The monocular visual field is the lateral visual field of each eye, in which there is no input from the other eye. The extent of the monocular and binocular visual fields is largely dictated by the location of the orbits and eyes in the skull.

Species with front-facing eyes have a large binocular visual field. Consequently, they have 2 small lateral monocular visual fields and a large posterior blind spot. Frontal eyes are found in predator species that require superior depth perception for accurate spatial localization when pouncing on their prey. Dogs, cats, and raptor birds fall into this category. The evolutionary price paid in the form of small peripheral fields and a large blind spot is of less concern to predator species.

On the other hand, herbivores have lateral orbits, giving them a small frontal binocular visual field and 2 large lateral monocular fields of vision that give them almost 360° panoramic vision. The large lateral monocular fields are important to these species as most of them need to see approaching predators. How do visual fields compare? The total visual field of cats is estimated at 200°, including a 140° frontal binocular field and 2 lateral monocular fields of 30° each (Figure 2). Horses are estimated to have a visual field of about 355°, including a frontal binocular field of 65° and 2 large lateral monocular fields of about 145° each. To know the implication of these numbers, consider that enucleation of 1 eye would cause a cat to lose 30° of its total visual field and a horse nearly 145° of its total visual field. With the loss of an eye, then, a horse could become dangerous and easily scared by objects moving on the side with vision loss.

PETS AND TV

When photoreceptors are stimulated by a flash of light, they need a minimum amount of time to recover before they can respond to a subsequent flash. If the flashes are presented rapidly, the photoreceptors do not have enough time to recover fully. Beyond a certain threshold, flashes become so rapid that the retina is unable to recover. At this point, the retina is no longer able to perceive or respond to the individual flashes, resulting in “fusion” of the responses and the perception of a continuous, rather than a flickering, light.

In humans, cone responses fuse at 45 Hz. Therefore, images projected on television or computer screens, which flicker at 60 Hz (in the United States), are perceived as a continuous image. But in many other species, cone responses fuse at 70 to 80 Hz. As a result, pets can perceive individual flickering images when watching television, which can have a dramatic effect on their interest in the program.

For the same reason, companion animals can detect the flickering of fluorescent lights. This is an important distinction that should be considered when selecting lighting for your hospital. Yellow, incandescent or LED bulbs that do not flicker provide the patient with a more hospitable atmosphere.

NIGHT VISION

The common narrative that companion animals have very sensitive night vision is based in truth. Study results show that cats can detect light that is 6 times dimmer than the lowest detectable threshold of humans (Figure 3).
This is due to several factors. First is the amount of light entering the eye. Cats have very large corneas and pupils, with diameters about 50% larger than those of humans. Therefore, more light can pass through feline eyes and reach the retina.

Second, with the exception of pigs, all domestic species possess a tapetum lucidum, a reflective tissue located in the choroid behind the retina. Light that is not absorbed by the retinal photopigment strikes the tapetum and reflects back to the retina, doubling the chances that it will be absorbed. Thus, the tapetum acts as a mirror that helps the animal increase retinal illumination in dim light. But there is an evolutionary price to be paid. The light reflected by the tapetum is scattered in the eye, reducing visual resolution. This has little consequence at night when cones, which are responsible for high-resolution vision, are inactive, but it becomes very detrimental in daylight.

The third and most critical factor that affects night vision is the distribution and concentration of retinal photoreceptors. In the retinal periphery, the maximal rod concentration in cats is about 5 times higher than that in humans. Because rods are much more sensitive to low light levels, and in fact can detect a single photon, this high rod concentration provides cats with their highly sensitive night vision and motion perception.

**VISUAL RESOLUTION AND ACUITY**

Visual resolution is determined mostly by the optics of the eye and the anatomy of the retina. Optically, in an emmetropic eye, light focuses properly on the retinal photoreceptors, contributing to a sharp image. In a short-sighted (myopic) eye, the image is focused in front of the retina, while in a far-sighted (hyperopic) eye the image is focused behind the retina, both of which result in a blurry image.

Findings from a study of 1500 dogs showed that a majority are emmetropic, meaning the optics of their eyes are calibrated to generate a focused image on the retina. If these dogs were humans, they would not require corrective glasses. The same study’s results showed that about 25% of all dogs are short-sighted, with a refractive error ranging from -0.5 to -6.0 D.

For some dog breeds, the average refractive error is myopic. For example, two-thirds of Rottweilers studied were short sighted, with a mean refractive error of -1.8 D. Similarly, significant numbers of dogs were far sighted, with certain breeds having a mean far-sighted refractive state. For example, the Australian shepherd has a mean refractive error of +1.3 D.

Visual resolution is also determined by retinal anatomy. As noted, factors that contribute to enhanced night vision have a detrimental effect on daytime vision and visual resolution. Thus, the presence of a tapetum lucidum in the eyes of dogs and cats causes scattering of light that reduces visual resolution. Furthermore, differences in the concentration of cones, which process high-resolution images, also affect visual resolution. In companion animals, the concentration of these cells is lower than in humans, resulting in lower visual resolution.

For example, the maximal cone concentration in the feline retina is one-eighth that in the human retina. Consequently, even if a dog or a cat is emmetropic, and has a well-focused image on the retina, its visual resolution will be reduced because the resolving power of the eye is attenuated by the low cone concentration in the retinas.

Visual acuity is typically expressed as a Snellen fraction, and this is where people have the advantage. The acuity of normal humans is the well-known figure, 20/20. By comparison, the visual acuity of horses is estimated to be 20/33, meaning that a horse must be 20 feet from an object to see it as well as a person standing 33 feet away can see it.

Visual acuity is 20/75 in dogs and 20/150 in cats. In other words, a cat has half the acuity of a dog and a fifth of the acuity of a horse. The simple translation: A cat has to be more than 7 times closer to an object to see it as sharply as we do! These figures are based on the assumption that the animal is emmetropic. If the animal is not emmetropic, then its visual resolution will be poorer.

It all seems so clear now, doesn’t it?

References available at AmericanVeterinarian.com.

Dr. Ofri is a professor of comparative ophthalmology at the Koret School of Veterinary Medicine, Hebrew University of Jerusalem in Rehovot, Israel.
Getting Started With Telemedicine

Giving clients access to you at their convenience offers a plethora of benefits for your patients, your clients, and your practice.

By Aaron Smiley, DVM

Eighteen months ago, I was introduced to a smartphone app that helps me build better client relationships, supports my patients’ health more effectively, and increases revenue for my practice. What kind of app was it? A telemedicine app.

As the chief of staff at 2 practices, I know firsthand that being accessible to clients at all hours to answer questions is one of the quickest ways to convert customers into enthusiastic advocates for the practice.

I initially became motivated to investigate telemedicine apps when I realized I was already practicing telemedicine on a routine basis. Any time I answered a text, a Facebook message, or a phone call from a client about their pet, I was practicing telemedicine.

Telemedicine is an overarching term that refers to all technology used to deliver health information or education remotely. According to the American Veterinary Medical Association (AVMA), telemedicine is exchanging medical information regarding a patient’s clinical health status from one site to another via electronic communications.

Improved technology now gives us the ability to practice telemedicine in much more effective ways because the app provides upfront guidelines, ensures confidentiality, and is compliant with state regulations. It also allows veterinarians to give clients access at the clinician’s discretion, which fosters a better work-life balance.

BENEFITS OF TELEMEDICINE

I’ve found that people want to be able to communicate with their health care professionals using the same technology they use to communicate with everyone else in their lives: their smartphones.

Offering clients more access to your practice, even if only to ask the simplest questions, can ease their anxiety and improve your relationship.

Although it may seem counterintuitive, implementing telemedicine in my practice has given me more free time. Surgery follow-ups, check-ins, and even writing prescriptions can be done via an app, allowing me to keep my clinic schedule open for patients that need to be seen on-site.

Telemedicine has also helped grow revenue. Once I let my clients with a valid veterinarian-client-patient relationship (VCPR) know that I can diagnose and prescribe through the app, they take to it quickly. Now, I do telemedicine consultations almost every day—and get paid for them.

WHAT TO LOOK FOR IN A TELEMEDICINE APP

Dozens of available apps offer a variety of telemedicine services. Based on my experience, the app you choose should incorporate these 4 key characteristics:

• **Legality:** Most states, as well as the AVMA, require a valid VCPR for a veterinarian to diagnose, prescribe medication, or otherwise treat an animal via telemedicine. Make sure you are using an app that allows you to connect with pet owners with whom you have an established VCPR.

• **Security:** Privacy is important. A viable telemedicine app should store all information securely to ensure client and patient privacy—and ideally is compliant with the Health Insurance Portability and Accountability Act.

• **Payment:** You will be giving clients the same level of service they would expect if they had come into the office, so you should charge them as such. Look for an app that allows you to bill clients directly through its interface so you won’t have to manage the billing on your own.

• **Accessibility:** You may be concerned that clients will be calling and texting you in the middle of the night. To prevent this, select an app that allows you to go offline so your clients know that you are not available to answer messages when you’re sleeping, eating dinner with your family, or taking a vacation, for instance.

Additional considerations come into play as well. Your telemedicine app should:

• Be specific for health care professionals.

• Allow clients to text, call, and send photos or videos of their pets.

• Offer a library of educational materials that can be sent to clients as needed.

• Be accessible via smartphone as well as desktop and compatible with both Android and iOS operating systems.

• Let you set pricing.

• Allow for multiple clinic users so that team members can answer basic questions.

• Integrate directly with your electronic health records system.

• Have real-time video calling capabilities.

• Offer excellent customer support.

Dr. Smiley is chief of staff at 2 veterinary practices in Indiana. He presented on the topic of telemedicine at the 2018 Veterinary Innovation Summit in College Station, Texas, and the Indiana Veterinary Medicine Association annual meeting, where he was named 2018 INVMA president. Dr. Smiley uses the Medici telemedicine app.
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Pay Your Self First
Attaining financial health requires a complex balance of spending some, saving more, being satisfied with less, and mitigating risks.

By Darby Affeldt, DVM

Where is it?” I asked frantically, searching under my desk, opening and closing drawers, and shuffling and reshuffling paperwork. A confused, bemused look came over my client’s face. “What on earth are you looking for?” she asked. “Your money! The money you should be accumulating each month based on your income and what you said you spend!” I responded. “I can’t find it anywhere.”

Silence filled the room, and then she burst out laughing—we both did. It was a moment of truth: She was spending too much money and, as a result, having trouble reaching her goals. After a minute of hearty laughter, she grew quiet and reflective. “I get it now,” she said, “and you’re absolutely right. I say I want to get out of debt, save more for my retirement and get myself on track, but I choose to spend on myself before anything else.”

Fortunately, we worked together to design a comprehensive strategy that aligned her budget with her goals and implemented a multifaceted savings strategy. After a year, she was in good financial shape. Sadly, though, this is not the case with all my clients. Destructive financial habits can cause irreparable damage to retirement income, and there isn’t always enough time to rectify the mistakes. As human capital—the ability to work and generate income—wanes over the course of a career, it will ideally be replaced with financial capital—growth from years of consistent savings—to enjoy a successful retirement. With proper strategies, future financial goals and dreams can be realized.

FINANCIAL SUCCESS REQUIRES DISCIPLINE
Saving money is comparable to physical fitness. Most people understand that losing weight or getting in shape is the result of eating a balanced diet and getting regular exercise. There’s really no mystery to it; yet many people struggle to manage their weight. It comes down to discipline, and human nature does not often tend toward discipline; people generally seek instant gratification. I like to think of financial health in the same way.

Getting into excellent financial shape is about discipline, and aside from the complexities of the financial road map, saving is just that simple. It is a choice.

Most people are familiar with the phrase “pay yourself first,” but it can be misleading. It’s intended to mean save first, yet people don’t adhere to it, or worse, they justify that it means spending on themselves first. Whether the challenge is spending too much or saving in the wrong way, I often come across clients who have not made saving a priority. Perhaps “pay your future self first” would inspire people to recognize that saving is not deprivation; it’s simply deferred spending.

In my experience, spending blindly or haphazardly is the main culprit of financial struggle. People simply don’t track their spending, so they don’t know where most of their income goes. Beyond overspending, there are a host of other reasons people don’t save. I have met many veterinary practice owners who aren’t overspending, at least not on themselves, but they are still not on track to meet their long-term financial goals. They work very hard, but because of poor practice management, their income drains away inefficiently and their practice may not be profitable as they’d like.

Sometimes healthy paychecks do come home, and people believe they are saving first, but they’re not necessarily saving in the right place, using the right strategy or talking to the right financial adviser. I’ve pored over countless investment portfolios with ill-fitted investments that resulted from poorly educated clients or bad advice.

It’s also not uncommon for parents to crush themselves financially to pay their children’s college tuition when multiple alternatives could have been implemented earlier to ensure this was not the case. Most often, when financial goals seem elusive, it’s due to a combination of reasons, which underscores the importance of working with an adviser who is trained to design a comprehensive financial blueprint.

ESTABLISHING YOUR UNIQUE APPROACH
There is no consistent rule of thumb when it comes to how much to save, how to save it, or where to save it. Each person’s situation is unique, and these decisions should be made in concert with the holistic picture, not unlike in veterinary medicine.

Early in their career, veterinarians may warrant only simple financial tips and guidance. As time goes on, however, it is wise to find an adviser who can offer comprehensive advice. Too many people allow dollars to steer their lives instead of becoming the drivers behind their own saving strategies. While saving and focusing on financial matters might not make the top 100 list of fun things to do, neither does cutting back on meal portions or jogging for the first time in years. Still, both require consistent discipline and effort—and pay off in the long run.

Consider writing your past self a letter detailing your concerns, advice, and lessons learned about financial choices that you could have changed but didn’t. Next, imagine what your future self would write to you. Your future will absolutely depend on the sum of your individual financial decisions today.
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A Picture Is Worth a Thousand Likes

Use these 3 winning Instagram strategies to attract more followers and gain new clients.

By Naren Arulrajah

With well over 2 billion monthly active users, Facebook may be the reigning king of social media, but it is not necessarily the most brand-friendly social network platform for businesses. Instead, Instagram is the rising star of the social sphere. The image-based network now has 10 times more brand engagement than Facebook and is expected to soon reach the billion-user milestone.

This growing platform is especially well suited for veterinary content. If you are wondering how many animal lovers and pet parents use Instagram, consider these numbers: There are more than 85 million posts tagged #catsofinstagram and 108 million tagged #dogsofinstagram, but just 4.5 million tagged #kiddosfinstagram.

If your practice doesn’t already have an Instagram account, the good news is that getting started is easy and business accounts are linked to Facebook pages. Simply log in to your personal Instagram account, go to settings and select “Switch to Business Profile.” If you administer multiple pages, you will need to select your veterinary practice from the list. Instagram will pull information from your Facebook page, so very little is needed to complete your business profile.

Now you have an account on an engagement-eager network with millions of pet lovers. How can you get their attention, build an audience and acquire leads?

CREATE AMAZING VISUALS

Because Instagram is a photo-sharing network, it should come as no surprise that a photo is the most important feature of any post. Every picture makes a statement. Poor-quality photos and uninspired clip art will appear unprofessional and sloppy. Try these tips to create top-notch imagery:

- **Use the right tools.** You can download apps such as Adobe Spark and Canva to create collages, memes, and more, and they require only minimal technical skills. Simply start with a template and customize it with your image, text, and practice logo.
- **Choose stock photos carefully.** When possible, steer clear of using stock photos. Original images are more authentic, interesting, and personalized. If you need a stock photo, make sure the picture is high quality and relevant to the post. Avoid overused images—if you recognize them from ads or memes, other people will too.
- **Hire a professional.** Do-it-yourself options are available, but for maximum customization and quality, consider hiring a professional photographer or graphic designer.
- **Don’t be basic.** Simple photographs are ideal for Instagram, but don’t be afraid to mix it up with funny pet memes, cartoons, quotes, and videos.

USE HASHTAGS CORRECTLY

Take advantage of hashtags to generate buzz around your brand and make your content more discoverable. Posts with 4 or 5 hashtags are about 60% more engagement than those with none.

Tips for choosing hashtags:

- **Do your research.** When you begin typing a hashtag, Instagram will generate a list of options and show the number of posts that already use each tag. You can also use tools such as hashtagify.me or hashtag.org (both subscription services) for in-depth hashtag research.
- **Be descriptive.** The more popular a hashtag is, the higher the competition for it will be. Additionally, the highest-rated tags tend to be general. For example, #cat is used in millions of posts, meaning you will quickly be crowded out of search results. On the other hand, #mammacat and #kittencare have around 1000 posts each, indicating a more targeted audience with less competition.
- **Use local hashtags.** General hashtags are used around the world, whereas location-specific tags will target people near your practice. If you are in a larger city, you will probably find a number of relevant tags that are already trending. For example, there are over 27,600 posts tagged #catsofseattle and more than 89,000 with #amidiods.
- **Create your own.** Generic hashtags (those not specific to your practice) aid discoverability, but branded hashtags draw people together around a specific topic. They are most often used with contests, promotions, special events and anything that will create social media conversations. For example, if you hold a free vaccination clinic, you might encourage people to share pictures of their vaccinated pets using a designated hashtag.
- **Use tags sparingly.** The Instagram audience is more tolerant of excessive hashtags than users of other networks. However, that doesn’t mean more is always better. Too many hashtags can make your post look spammy and unprofessional, especially if they’re not relevant to the image.

RUN CONTESTS

This is probably the fastest way to generate buzz on Instagram. The simplest contests can be administered manually. For more complex promotions, or those attracting a high number of entries, consider purchasing a subscription to contest management software such as Wishpond or Woobox.

Before you launch a promotion, check your local laws. Depending on your location, accidentally stepping over a legal line may be surprisingly easy, even for a contest with a very modest prize. Additionally, familiarize yourself with Instagram’s rules. They are rather basic, but you should take the time to read and understand the latest guidelines before you get started.
Considering these hashtag numbers, it’s clear how many pet lovers use Instagram.

108 million
#dogsofinstagram

85 million
#catsofinstagram

4.5 million
#kidssofinstagram

Once you know what you can do, it’s time to create your contest. Start by identifying a goal and choosing a relevant theme. If you want to attract cat owners, for example, you might have a contest for the funniest cat photo.

The next step is creating your own rules and guidelines. Summarize them in 1 or 2 lines for inclusion in contest promotions, and make a detailed version available on your website. Rules should include:

• **Prize.** The best option is usually a gift certificate for your practice or a free sample of a product you sell.

• **Entry eligibility.** Decide what qualifies as an entry and whether there are restrictions. For example, in a photo contest, each picture is an entry. You might require that the image be original and inoffensive and include a pet. Alternately, in a “caption this” contest, each suggested caption is an entry. You might include an acceptable character count and forbid explicit words.

• **Participant eligibility.** Are there age restrictions? Can people enter more than once? Is the contest open to the public or just your clients?

• **How to enter.** The simplest Instagram photo contest requires a participant to share a photo, tag your practice, and include a branded hashtag. There are other options, such as requiring a like or comment and allowing entries on other networks. However, you cannot ask people to tag others who are not actually in the picture.

• **Judging.** Who will choose the winner? If the voting is going to be public, will you provide an online ballot, count likes, or use another voting system? What will you do if there is a tie?

• **Dates.** You need to establish when you’ll begin accepting entries, the final deadline, when voting will begin and end, and when the winner will be announced.

The internet loves pictures of animals, making Instagram an ideal marketing opportunity for veterinarians. If you aren’t making use of it, now is the time to start.

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Mr. Arulrajah is president and CEO of Ekwa Marketing, a complete internet marketing company that focuses on SEO, social media, marketing education and the online reputations of veterinarians/practice owners. With a team of 180+ full-time marketers, ekwa.com helps practice owners who know where they want to go, get there by dominating their market and growing their business significantly year after year. If you have questions about marketing your practice online, call 855-598-3320 to speak one-on-one with Naren.

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Animals and Airplanes: The Veterinarian’s Role

How do new airline regulations regarding the types of animals allowed to fly in cabins affect veterinary practitioners?

By Debra Vey Voda Hamilton, Esq.

In recent months, many major airlines have tightened their regulations regarding service and emotional support animals traveling on board flights—actions that have raised a number of questions for veterinarians:

- How can veterinarians protect themselves while assisting pet owners in caring for these animals?
- How do you provide health care to the pet yet not give an evaluation of its behavior or training?
- What is the veterinarian’s role in this 2-sided pet care question?

At the recent Animals on the Mind 3.0 conference, hosted in May by the Institute for Human-Animal Connection, nonveterinarian experts in the field of human-animal interaction spent 2 days exploring these questions. Psychologists, animal trainers, and service/support animal handlers shared their perspectives on identifying these pets while caring for both the person and the animal.

No one disputes the benefits available to people who use service or support animals. Because these animals come in all shapes and sizes with varying training levels and abilities, however, the temptation to abuse the privilege is always present.

At the conference, presenting researchers and service, emotional support, and therapy dog users were careful to point out how the handler/animal team works. They clearly had a deep awareness of the needs of the animal in these interdependent relationships. To them, the pets’ needs were as important as any human therapeutic benefits that resulted from these relationships.

Given these studies, completed on a much more evaluative level of observation of the training and behavior of the animal and the handler, how can veterinarians adequately observe and evaluate a pet being asked to do tasks? Is it even their role as health care providers to make such an evaluation during a pet’s pretravel health check? Questions involving the legitimacy of a service, emotional support, or therapy pet or its ability to behave on a plane creates a conundrum for the veterinarian.

In early March, the American Veterinary Medical Association (AVMA) announced that it had reached an agreement with United Airlines to revise the carrier’s Veterinary Health Form, which is now required prior to flying with a service or emotional support animal. The AVMA contended that the information being requested in the original version of the form might not position United Airlines to make good decisions that would support the health and welfare of both human and animal passengers. The AVMA also expressed concern that the statements on the form created potential liability risks for veterinarians attesting to them. In reality, veterinarians cannot and should not vouch for the training or behavior of any animal in their practice. It is beyond the scope of their examination, training, and expertise. What a veterinarian observes about a dog in the confines of a veterinary hospital might be quite different from how the dog reacts in a pressurized, noisy airline cabin.

Now the question remains: How can veterinarians serve their clients and themselves when it comes to providing a health check of a service or emotional support dog?

First, it’s important to understand the differences between a service animal and an emotional support animal. Service animals, which are acquired after months of individualized and partnership training, have federally protected rights under the Americans With Disabilities Act. They must be granted reasonable access anywhere.

An emotional support animal has protected access under the Fair Housing Act and Air Carrier Access Act, passed in 1988 and 1986, respectively. Reasonable accommodations must be made upon proof that the pet provides a necessary service. Emotional support animals provide a service by their mere presence; no real training is required. For emotional support animals to fly in the cabin of a plane, a doctor’s note identifying the support the animal provides and the symptom(s) it ameliorates is mandatory.

Many veterinarians feel compelled to verify a service animal’s training and behavior, but this is not within the scope of their training. Instead, they should explain to their clients that they can only sign the health voucher. It is all they can uniquely do with their training and expertise.

Now that the AVMA has helped United Airlines reshape its form, it also hopes to work with other airlines to create more appropriate veterinary health forms, ensuring the safe travel of service and emotional support animals while keeping passengers and crew members protected.

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Important Safety Information

Mirataz™ (mirtazapine transdermal ointment) is for topical use in cats only under veterinary supervision. Do not use in cats with a known hypersensitivity to mirtazapine or any of the excipients. Do not use in cats treated with monoamine oxidase inhibitors (MAOIs). Not for human use. Keep out of reach of children. Wear gloves when handling/applying, wash hands after and avoid contact between the treated cat and people or other animals for 2 hours following application. Use with caution in cats with hepatic and kidney disease. Cat’s food intake should be monitored upon discontinuation. Safety has not been evaluated in cats less than 2 kg, less than six months of age or in breeding, pregnant or lactating cats. The most common adverse reactions observed during clinical trials were application site reactions, behavioral abnormalities (vocalization and hyperactivity) and vomiting. For additional safety information, see brief summary of prescribing information on page 33.


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1. Data on file. Zoetis Market Research: Blood Glucose Monitoring Report, July 2017. Zoetis Inc. All trademarks are the property of Zoetis Services LLC or a related company or a licensor unless otherwise noted. © 2017 Zoetis Services LLC. All rights reserved. ATK-00175