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VETERINARY REFERRAL NEWS FROM ANGELL ANIMAL MEDICAL CENTER

INTERNAL MEDICINE

Immune-Mediated Hemolytic Anemia (IMHA) in Dogs

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Immune-mediated hemolytic anemia (IMHA) is a common immune-mediated disease in dogs and an important cause of severe anemia. IMHA occurs when autoantibodies are formed against red blood cells, leading to their destruction by phagocytic cells in the liver and spleen (extravascular hemolysis) or by complement proteins within blood vessels (intravascular hemolysis). This results in a rapid onset of potentially life-threatening hemolytic anemia.

Although IMHA can occur in any dog, one large study noted that purebred dogs represented 89% of all cases, with cocker and springer spaniels being overrepresented.[1] Clinical signs of IMHA are often non-specific, including lethargy, inappetence and weakness. Owners may notice jaundice, particularly of the gums, sclera, pinnae, or poorly haired areas of the body such as the ventral abdomen. In cases of intravascular hemolysis, owners may notice discoloration of the urine secondary to hemoglobinuria. A physical exam may reveal an enlarged spleen and liver, which can occur secondary to both extravascular hemolysis and extramedullary hematopoiesis. Fever is frequently present due to the severe systemic inflammatory

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ANESTHESIA

The Basics of Locoregional Anesthesia

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Locoregional anesthesia has been widely used in human medicine for decades in a wide array of procedures, including orthopedic surgeries, oncologic surgeries, abdominal procedures and even laparoscopic procedures. Regional anesthesia has been shown to reduce risks associated with general anesthesia by decreasing the amount of anesthetic needed, to improve intraoperative analgesia, and to improve postoperative comfort and recovery.[1] Recently, there has been an increase in interest in locoregional anesthesia in veterinary medicine and a surge in the number of articles in veterinary literature. The focus of this article will be to review the basics of local anesthetics used in clinical practice, to discuss the techniques used to perform regional anesthesia, and to give examples of some of the more commonly used techniques in veterinary medicine. The

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INSIDE: REFERRAL CONTACT INFO AND UPCOMING CES ON A REMOVABLE POSTCARD

Immune-Mediated Hemolytic Anemia (IMHA) in Dogs

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FIGURE 1

↘ Severe icterus and pallor of mucous membranes in a dog with IMHA.

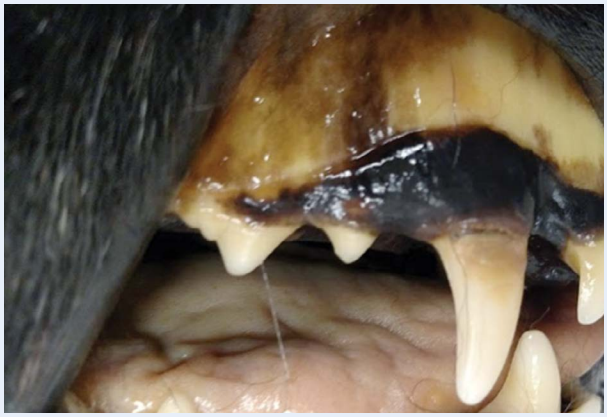
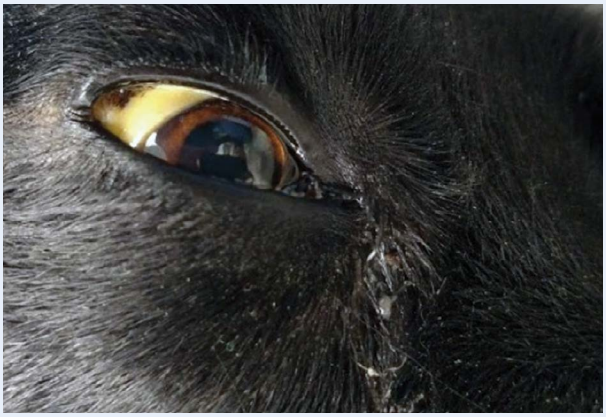


FIGURE 2

↘ Severe icterus of the sclera in a dog with IMHA.



response, and compensatory responses to anemia, such as tachycardia and tachypnea, are common.

IMHA should be considered as a differential diagnosis in any dog with an acute onset of anemia that has evidence of hemolysis. An immune-mediated pathogenesis is supported by the presence of significant spherocytosis, a positive saline agglutination test or a positive Coombs test. Any of these factors, combined with evidence of hemolysis, such as hyperbilirubinemia, ghost cells, hemoglobinemia or hemoglobinuria, is considered strong evidence for IMHA. Although most dogs with IMHA have a strongly regenerative anemia, approximately 30% will not have evidence of regeneration at the time of diagnosis.[2] In the majority of these dogs, this is due to the anemia being "pre-regenerative," meaning the bone marrow has not had adequate time to mount a regenerative response.

Although most cases of IMHA are considered primary, as they have no established underlying cause, some dogs with IMHA may develop the disorder secondary to another disease process. While many vector-borne diseases have been implicated in the development of IMHA, only babesosis has strong evidence of truly causing IMHA in dogs. Other vector-borne pathogens, including *Leishmania*, *Bartonella* and heartworm, have been associated with Coombs-positive anemia, while others, such as *Anaplasma*, have been noted concurrently in patients with IMHA. The causal relationship of these infectious agents with IMHA has not been established, but treatment of infectious comorbidities is still an important part of therapy.[2] In areas like New England where tickborne infections are common, treatment with doxycycline while awaiting results of tick testing is a common and prudent practice. Although babesiosis is a relatively uncommon infection, testing should be strongly considered in any dog with IMHA, particularly in overrepresented breeds, such as pit bull terriers. There have been anecdotal associations of several types of cancer with IMHA, so imaging of IMHA patients with abdominal ultrasound and thoracic radiographs is often performed. An abdominal radiograph to rule out zinc foreign bodies, such as coins, that could lead to hemolysis is also an important diagnostic step. Unlike immune-mediated thrombocytopenia (ITP), there is not strong evidence of medications acting as triggers for IMHA, although drug-induced IMHA may still be possible. Similarly, no definitive link between vaccination and IMHA has been established.[2]

IMHA is treated with immunosuppressive medications, anti-thrombotic medications and supportive therapy, including blood transfusions. Multiple blood transfusions are often needed to stabilize the patient while waiting for immunosuppressive medications to take effect. Steroids are the mainstay of treatment for IMHA, with recommended starting doses of prednisone of 2 mg/kg/day, or 40-60 mg/m^2, for dogs >25 kg. Secondary immunosuppressive drugs, such as cyclosporine and mycophenolate, are frequently used, although there is no strong evidence of a beneficial effect with any of these medications. It is generally not recommended to use more than two immunosuppressive medications together due to the significantly increased risk of infectious complications. Since cyclophosphamide has been shown to potentially worsen outcomes in IMHA patients, this medication is not recommended.[3]

In cases of severe or refractory disease, more aggressive treatments may be considered. Human intravenous immunoglobulin (hIVIG) has been used as a salvage treatment for IMHA, although a survival benefit has not been established. Splenectomy has also been used in cases of refractory IMHA and has been shown in some studies to result in reduced medication and transfusion requirements.[3] Therapeutic plasma exchange is a newer therapy to remove autoantibodies in IMHA patients and shows promise in stabilization of severe or refractory cases of IMHA.

Anti-thrombotic medications are an important part of therapy for IMHA, as thromboembolism is a leading cause of death in these patients. Because venous clots (particularly pulmonary thromboembolism) are most common in IMHA patients, anticoagulant medications, such as heparin, may have better efficacy than anti-platelet agents, like clopidogrel or aspirin.[3] However, since heparin should ideally be adjusted in each individual patient based on measurement of anti-factor Xa levels, this is not a practical option for most patients. Rivaroxaban is a newer oral factor Xa inhibitor that is used in human medicine to prevent venous thrombosis without requiring monitoring of anti-factor Xa levels. Although rivaroxaban has not yet been widely used in canine IMHA patients, one small study did show it was well-tolerated and not associated with bleeding complications in this patient population.[4] This medication is currently prohibitively expensive for many veterinary patients but may become a better option in the future if generic versions become available.

Because of the current practical limitations associated with anticoagulant medications in veterinary patients, most dogs with IMHA are given clopidogrel or aspirin to try to prevent thromboembolism. Clopidogrel (1.1-4 mg/kg once daily) is the preferred choice over aspirin, both because of unpredictable platelet inhibition for low doses of aspirin and a higher likelihood of inducing gastrointestinal bleeding if aspirin is used.[3] A recent study showed that in healthy dogs, clopidogrel alone is not associated with

INTERNAL MEDICINE

Immune-Mediated Hemolytic Anemia (IMHA) in Dogs

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development of GI bleeding, and its use in addition to prednisone does not increase GI bleeding risk compared with prednisone alone.[5] However, administration of aspirin alone was associated with GI bleeding in healthy patients. Furthermore, dogs that received aspirin and prednisone together had more severe lesions on endoscopy after two weeks of treatment than dogs receiving prednisone alone.[6] Generic clopidogrel is widely available and inexpensive, making it simple to use for most owners.

The prognosis for patients with IMHA is guarded, with mortality rates of 50% and relapse rates of 6% – 13% commonly reported.[7] Patients are at greatest risk during the acute phase of treatment, when immunosuppressive medications have not yet reached full effect and the risk for thromboembolic disease is highest. However, patients that make it through this period may have prolonged survival with appropriate continued therapy and monitoring. In general, the dose of prednisone should be reduced every three weeks as long as the hematocrit remains stable above 30%, and evidence for ongoing hemolysis (such as spherocytosis) is minimal. It is recommended to continue anti-thrombotic medication until prednisone has been discontinued, since use of steroids is associated with increased risk of thrombosis. If secondary immunosuppressive drugs, such as cyclosporine or mycophenolate, are used, they are typically tapered or discontinued only after patients have been successfully weaned off of prednisone. Due to the slow nature of the taper recommended for IMHA, owners should be prepared for patients to be on immunosuppressive medications for at least three to six months.[3]

IMHA is a serious disease, with death frequently occurring from thromboembolic disease or severe anemia. However, patients treated appropriately and aggressively that make it through the initial period of hospitalization may have prolonged survival with a good quality of life.

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6 Clinical, clinicopathologic, and gastrointestinal changes from aspirin, prednisone, or combination treatment in healthy research dogs: a double-blind randomized trial. Whittemore, J.C., et al. *J Vet Intern Med*. 2019;33:1977-1987.

7 Systematic review of evidence relating to the treatment of immune-mediated hemolytic anemia in dogs. Swann, J.W., and Skelly, B.J. *J Vet Intern Med*. 2013;27:1-9.

↘ Continuing Care During COVID-19 Crisis

Recognizing the importance of managing chronic disease and conditions, Angell has put changes into place so we can ensure the best long-term outcome for patients while continuing to serve our referring partners and keeping our staff and clients protected.

Referral Cases to Waltham and Boston

We are welcoming all referral cases at our Waltham and Boston locations for all of our services. Please call **617-522-5011**, call the specialty service directly, or visit **angell.org/referrals**.

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As always, our emergency room is open 24 hours a day, 7 days a week at our Angell Boston and Angell Waltham locations to care for our most acutely ill patients.

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We are offering urgent care appointments for patients who have non-life threatening but urgent issues. Please call our referral line at **617-522-5011**. Clients can call **617-522-7282**.

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Angell continues to fill prescriptions 7 days per week. Curbside pick-up and mailing of prescriptions are both available (shipping fees apply). Clients can submit their prescription requests at **angell.org/pharmacy** or by calling **617-524-5700**.

We continue to use a concierge approach to help ensure Angell's clinicians and staff can safely deliver care to patients. Details on this approach are posted at **angell.org/COVID**.

Though clients are asked to remain outside the building and we have cancelled visitation of hospitalized patients, we continue to text pictures and updates so clients can stay in close contact with their pets while they are hospitalized. The only visiting exceptions are for end-of-life scenarios.

Our clinics, Angell at Nashoba (Westford, MA) and Angell at Essex (Danvers, MA) remain open.

ANESTHESIA

The Basics of Locoregional Anesthesia

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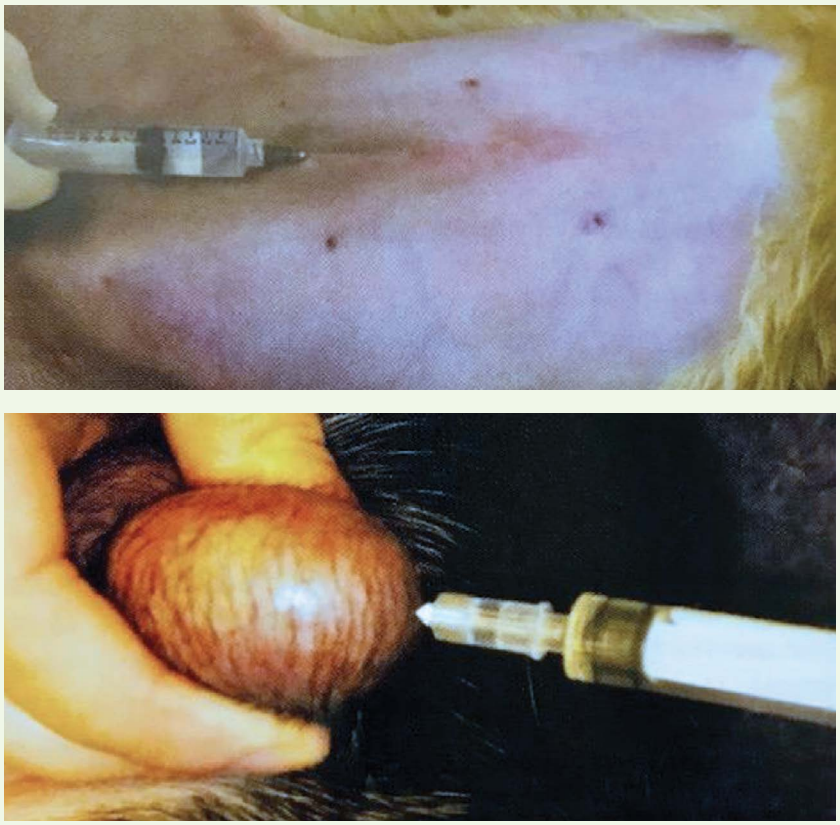
FIGURE 1

↘ The top picture shows the proper subcutaneous administration of a local anesthetic at midline, spanning from umbilicus along the anticipated incision length. The bottom picture shows the administration of local anesthetic into the body of the testicle and away from the epididymis. Grimm KA, Lamont LA, Tranquilli WJ, Greene SA, Robertson SA, ed. Veterinary Anesthesia and Analgesia: The Fifth Edition of Lumb and Jones; Wiley Blackwell. 2015.



specific steps to perform each type of block are beyond the scope of this article and can be found in both textbooks and the literature.

Local anesthesia results from the blockade of nerve impulses to abolish sensation. All currently available local anesthetics are either aminoesters or aminoamides. Local anesthetics work by preventing electrical impulse conduction by membranes of nerves and muscle. They can be applied topically, injected around peripheral nerves or major nerve trunks, or administered within the epidural or subarachnoid spaces. Local anesthetics act mainly on voltage-gated sodium channels blocking inward movement of sodium, thereby impeding membrane depolarization and nerve excitation and conduction. Local anesthetics express what is called a differential pattern of sensory and motor blockage: first vasodilation occurs, followed by loss of sensation of temperature, sharp pain, light touch and, lastly, loss of motor activity.[2] In addition to blocking sodium channels, local anesthetics also inhibit other ion channels, such as potassium or calcium channels, at the level of the spinal cord, which most likely contributes to their nociceptive effects. Local anesthetics commonly used today are for the most part amides and include lidocaine, bupivacaine, ropivacaine and mepivacaine. Lidocaine is one of the most commonly used local anesthetics and has a rapid onset of action and a duration of action of one to two hours.[3] Lidocaine can be used for peripheral nerve blocks and epidurals, and systemically. The toxic dose of lidocaine in dogs is 6 – 10 mg/kg and in cats is 3 – 5 mg/kg.[2] Bupivacaine is also very commonly used in small-animal medicine and has a slower onset of action of about 20 minutes and a longer duration of action of eight to 12 hours.[3] Unlike lidocaine, bupivacaine cannot be given intravascularly and is reserved for local blocks and epidurals only. Ropivacaine and mepivacaine are more commonly used in large-animal medicine and surgery.

Many factors affect the onset and duration of local anesthetics, including pKa, protein binding, liver and renal function, age of patient, vascularity of tissue site, pregnancy status and presence of additives. It is important that the veterinarian is familiar with the comorbidities of the patient for whom a local anesthetic will be used. Both renal and hepatic dysfunction can lead to accumulation of local anesthetics and an increased risk of toxicity because of reduced metabolism and excretion (of the parent drug and active metabolites).[2] Signs of toxicity include CNS signs and cardiovascular collapse. CNS signs follow a progression and include anxiety, mild sedation, ataxia, muscle twitching and seizures. These signs are thought to precede the signs of cardiovascular toxicity. Cardiovascular collapse is due to the binding of cardiac sodium channels, and signs include arrhythmias, hypotension, bradycardia, reduced myocardial contractility and asystole. The treatment of local anesthetic toxicity includes supportive care, such as oxygenation and ventilation, and possibly lipid treatment.

Many different types of locoregional anesthesia can be employed in everyday practice, ranging from simple blocks, such as line blocks, to more complicated blocks, such as those requiring an ultrasound or a nerve stimulator. Rarely is there a surgery or procedure for which the patient will not benefit from the addition of a local block, as it is often fast and easy to perform and also inexpensive. Simple blocks that can be performed in general practice on a daily basis include line blocks for ovariohysterectomies, testicular blocks for castrations, wound infiltration, and ring blocks for procedures distal to the carpus or tarsus. These blocks can be performed by both technicians and doctors (Figure 1) and provide excellent patient comfort and reduced postoperative use of opioids.[4] Drug choice for these simple blocks depends on time to initial incision, intended or needed duration of analgesia, and the invasive nature of the procedure. Lidocaine is often a good choice if the procedure will occur only a few minutes after the block, such as with wound infiltration. Bupivacaine is commonly used for testicular blocks and incisional blocks, as it provides a longer duration of analgesia than lidocaine, which is warranted in painful procedures. When performing any local block, it is of utmost importance to always avoid intravascular and intraneural injections. The addition of an intraperitoneal block to any spay or abdominal procedure has also been shown to reduce postoperative pain and opioid consumption in both human and veterinary patients.[5] Intraperitoneal blocks are easily performed by splashing 1.5 to 2 mg/kg bupivacaine onto the peritoneal surfaces, where vast numbers of nociceptors are present.

ANESTHESIA

The Basics of Locoregional Anesthesia

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In addition to simple blocks, more complicated blocks are performed by anesthesiologists using ultrasound guidance or nerve stimulator localization. Special needles are used when performing both ultrasound-guided and nerve stimulator-guided nerve blocks. When performing ultrasound-guided nerve blocks, echogenic needles are used to allow for easier visualization of the needle and more accurate delivery of the local anesthetic around the nerve (Figure 2). When performing blocks using the nerve stimulator, needles insulated (most often with Teflon) over their entire length are used to allow the electricity to exit only from the tip of the needles, allowing precise nerve localization (Figure 3). Locoregional anesthesia using the ultrasound or nerve stimulator or a combination of both allows anesthesia and analgesia to be provided to almost any part of the body. Commonly performed blocks at our hospital are performed using the nerve stimulator and include femoral/sciatic nerve blocks (Figure 4), providing anesthesia and analgesia to the stifle and anything distal to it; brachial plexus blocks, providing anesthesia and analgesia to the distal humerus and anything beyond it; and RUMM blocks, providing anesthesia and analgesia to the distal radius/ulna and anything beyond it. Lumbosacral epidurals are commonly used to provide anesthesia and analgesia for abdominal procedures, pelvic fractures, tibial-plateau-leveling osteotomies (TPLOs), any painful procedure involving the hind limbs and amputations. Caudal epidurals can be performed with or without a nerve stimulator at S3-Cd1 or Cd1-Cd2 and provide perineal, rectal, and vaginal/vulvar anesthesia and analgesia.

Locoregional anesthesia is an underutilized mode of providing excellent analgesia and an improved patient experience overall. Anesthesiology and pain medicine in humans are trending heavily toward performing as many procedures as possible under sedation and locoregional anesthesia, and hopefully veterinary medicine will follow in their footsteps.

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FIGURE 2

↘ Ultrasound appearance of the femoral nerve located at the femoral triangle. This is the target nerve for perineural administration of local anesthetic when providing anesthesia/analgesia to the stifle and distal. Grimm KA, Lamont LA, Tranquilli.

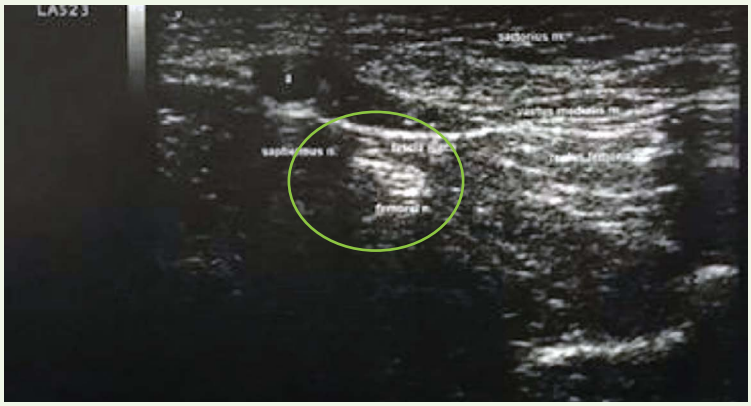


FIGURE 3

↘ Location of insulated needle insertion during performance of femoral lock. Grimm KA, Lamont LA, Tranquilli WJ, Greene SA, Robertson SA, ed. Veterinary Anesthesia and Analgesia: The Fifth Edition of Lumb and Jones; Wiley Blackwell. 2015.

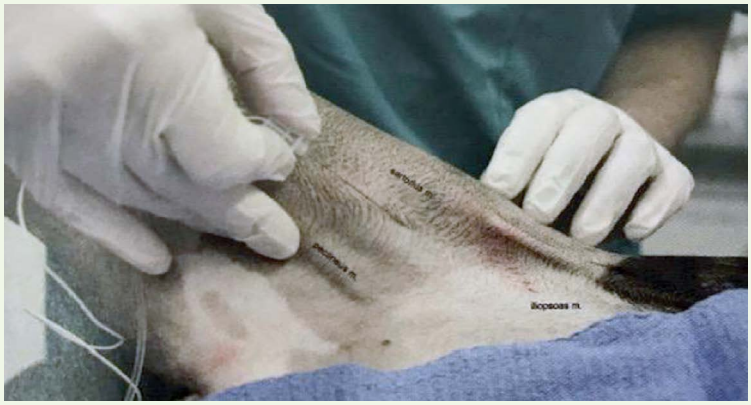
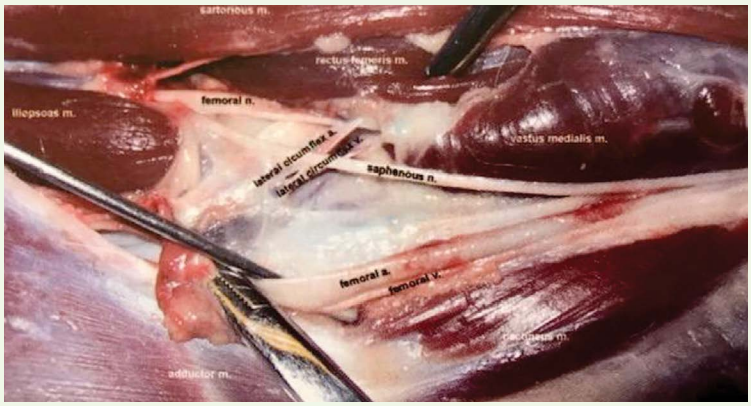


FIGURE 4

↘ Location of insulated needle insertion during performance of femoral lock. Grimm KA, Lamont LA, Tranquilli WJ, Greene SA, Robertson SA, ed. Veterinary Anesthesia and Analgesia: The Fifth Edition of Lumb and Jones; Wiley Blackwell. 2015.



Volumetric Modulated Arc Therapy (VMAT)

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angell.org/oncology | 617-541-5136

Volumetric modulated arc therapy (VMAT) or RapidArc® Radiotherapy Technology is an innovative form of intensity-modulated radiation therapy (IMRT) that delivers precise continuous radiation in a single or multi-arc treatment to the patient. With conventional IMRT techniques like step-and-shoot, the machine must make repeated stops and starts to treat the tumor from a number of different angles, generally over 5 – 10 minutes. In comparison, VMAT can deliver the dose to the entire tumor in a 360-degree rotation, typically in under two minutes.

Intensity-modulated radiation therapy is a type of highly conformal radiotherapy that shapes the radiation beam to closely fit the tumor, thus minimizing the dose to the adjacent normal tissues. To achieve such conformability, the linear accelerator uses a device called a multileaf collimator (MLC), which consists of thin leaves that move independently and form shapes that fit precisely around the treatment area. For reference, visit angell.org/IMRT.

VMAT is predominantly useful for delivering radiation therapy to tumors adjacent to sensitive body organs and can be an effective treatment for many types of cancer. This is particularly important in terms of late-term side effects. As our oncologic treatments are advancing, the potential for long-term survival increases, and thus our patients may live long enough to endure such side effects.

In addition to preventing permanent late-term side effects, VMAT has the added benefit of faster treatment times. In veterinary medicine, our patients are immobilized with heavy sedation or general anesthesia. While all precautions are in place to minimize adverse anesthetic events, short anesthesia times are always advantageous in patients receiving multiple treatments.

This technology can be used for fractionated as well as hypofractionated treatments, such as stereotactic body radiation therapy and stereotactic radiosurgery.

Currently, there are two reports of VMAT used in veterinary medicine. The first was VMAT-SBRT (Stereotactic Body Radiation Therapy) for adrenal tumors with vascular invasion. This study reported on nine dogs: three dogs were affected by cortisol-secreting adrenal tumors, and six dogs had non-secreting adrenal tumors treated with VMAT-SBRT. The median overall survival time was 1,030 days, and the overall mean reduction of the diameter and volume were approximately 32% and 30%, respectively. The endocrine profile normalized in two dogs with cortisol-secreting adrenal tumors. Side effects were mild and self-limiting.

The second study reported on 10 patients with brachial plexus tumors and found all treated patients showed a partial response and partial or complete reductions of neurological deficits, although local recurrence was observed in nine of 10 treated dogs. The mean overall survival of 371 days and mean progression-free survival of 240 were reported, which were comparable to reports with surgery alone. No side effects directly related to treatment were observed. This study concluded that VMAT can be a safe and viable alternative to surgery in cases of canine brachial plexus peripheral nerve sheath tumors (PNSTs) involving the proximal nerves and nerve roots.

Other tumor types being treated at our institution as well as other VMAT sites include brain and spinal cord tumors, trigeminal nerve tumors, adrenal tumors, primary bone tumors, nasal tumors, oral tumors, heart base tumors, urogenital tumors, anal sac tumors and intrathoracic/mediastinal tumors.

As more institutions gain the ability to use advanced technologies such as VMAT, more studies will be underway to expand our ever-growing understanding of the best utilization.

We are very fortunate to be within the first five veterinary institutions in the world to offer VMAT. If you have any questions regarding the therapy or tumor types treated with VMAT or radiation therapy in general, please contact the oncology service at oncology@angell.org.

↘ Picture of a patient that received VMAT-IMRT for a presumed meningioma and an incidental thyroid tumor. The axial image with a color-wash dose distribution (red is goal, and blue is lowest dose of radiation). The yellow rings represent the beam rotating 360 degrees around the two tumors.

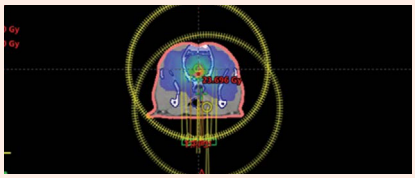


FIGURE 2

↘ The axial image with a color-wash dose distribution (red is goal, and blue is lowest dose of radiation). The yellow rings represent the beam rotating 360 degrees around the two tumors.

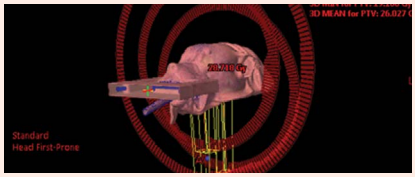


FIGURE 3

↘ The coronal image; yellow lines represent the beam angles.

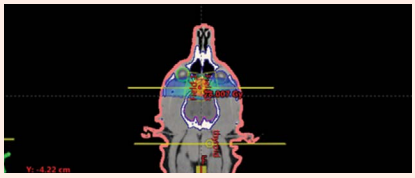
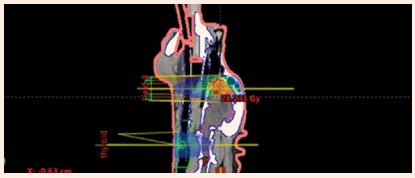


FIGURE 4

↘ The sagittal image showing the beam angles and color-wash.



Post-Cardiac Arrest

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INTRODUCTION

Cats and dogs have only a 6% – 7% rate of survival to discharge following cardiopulmonary arrest (CPA).[1,2] In CPA, there are two main phases of patient loss. The first phase is during initial CPA when the patient does not have return of spontaneous circulation (ROSC), in which about 65% of patients will be lost. The second phase of patient loss is after ROSC. Of those patients that have ROSC, about 85% will be euthanized or die before hospital discharge (Figure 1).[1,2] It is during this time that interventional strategies after ROSC have the potential to save more lives. Given the complexity of these cases, post-cardiac arrest patients require intensive monitoring in a 24-hour critical care facility to prevent re-arrest and to manage post-cardiac arrest syndrome.

POST-CARDIAC ARREST SYNDROME: DEFINITION AND PATHOGENESIS

Post-cardiac arrest (PCA) syndrome is a complex pathological response that occurs as a sequela to global body ischemia followed by reperfusion. The four main components of PCA syndrome include brain injury, myocardial dysfunction, systemic ischemia/reperfusion injury and pre-existing comorbidities.[2,3,4]

While ischemia creates the initial insult, paradoxically, it is the return of perfusion that causes further damage to the organ itself and may induce systemic damage to distant organs (Figure 2). Ischemia is when oxygen supply is less than the demand needed for normal tissue function.[4] It results in anaerobic glycolysis and significantly decreased production of energy to only two ATP and lactate. Elevating lactate levels will lower the pH in the tissue, which feedbacks negatively to inhibit ATP production. ATP is broken down to hypoxanthine and xanthine, which later becomes important in reperfusion injury and the production of free radicals. With no ATP production, the Na-K ATPase and calcium membrane pumps no longer work. This results in an influx of intracellular water and cellular swelling.[4] Increased intracellular calcium results in conversion of the enzyme xanthine dehydrogenase to xanthine oxidase. With the return of blood flow, there is an influx of oxygen into the tissues, which catalyzes xanthine oxidase to degrade hypoxanthine and xanthine, thus liberating the highly reactive superoxide anion (O2-) and uric acid as byproducts. Superoxide is subsequently converted to the hydroxyl radical (OH-) and consequently results in peroxidation of the cell's lipid membranes and in the production and systemic release of pro-inflammatory eicosanoids, disruption of cell permeability and, ultimately, cell death.

Neuronal tissue is sensitive during anaerobic glycolysis, and will deplete its ATP resources within 2 – 4 minutes compared with 20 – 40 minutes in the gastrointestinal tract and myocardium.[2] Myocyte dysfunction results from ischemia and reperfusion similar to what occurs at the cellular level in the nervous system.[2] Neuronal injury can manifest as delirium to coma, seizures, myoclonus, cognitive dysfunction, cortical blindness or brain death. Myocardial dysfunction is characterized by increased central venous pressure and can clinically manifest as reduced cardiac output, arrhythmias, hypotension, cardiogenic shock or even cardiovascular collapse in severe cases.[2,3]

FIGURE 1

↘ Two phases of patient loss (From Silverstein: Small Animal Critical Care).

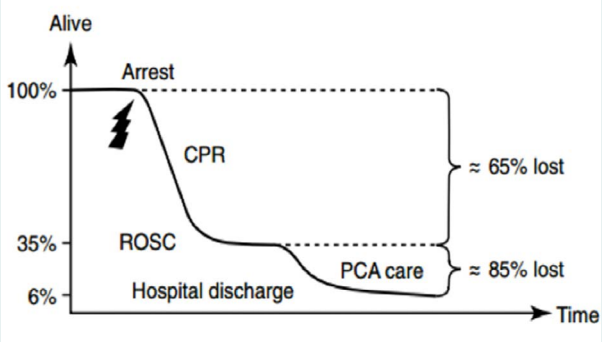
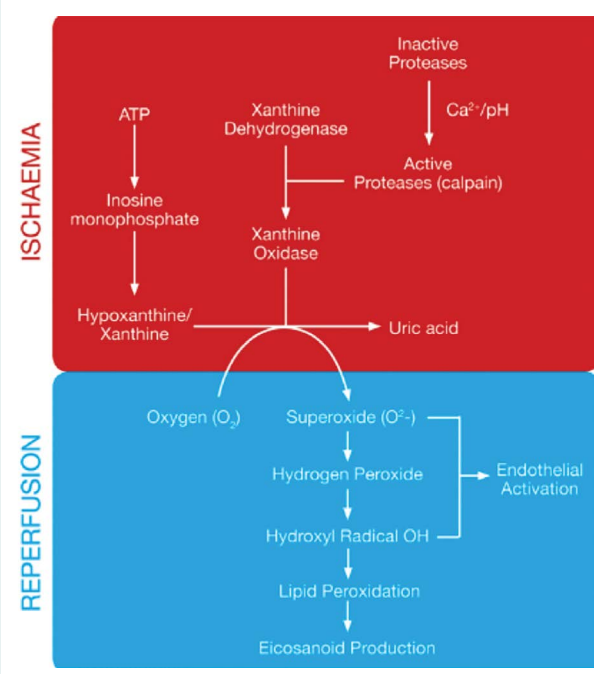


FIGURE 2

↘ Ischemia and Reperfusion Injury (From Cowled: Mechanisms of Vascular Disease).



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TARGETED THERAPY

Monitoring of the post-cardiac arrest patient uses the same principles as those you would apply to the critical patient. The goal immediately after ROSC is to sustain spontaneous circulation and perfusion of vital organs (e.g., brain, myocardium), attenuating further injury and preventing re-arrest.

"Sepsis-like syndrome"

Systemic ischemic-reperfusion injury is a sepsis-like syndrome because it shares many of its characteristics in relation to coagulation, inflammation and the endothelium. Treatment is highly individualized but is similar to sepsis therapy and targeted at early hemodynamic optimization, glycemic control and situational adrenal dysfunction (critical illness-related corticosteroid insufficiency, or CIRCI). Hemodynamic goals to reach are a mean arterial pressure of 80 mmHg or higher, a central venous oxygen saturation of 70% or more, and a lactate less than 2.5 mmol/L.[5] Strategies include the administration of intravenous fluids with the addition of vasopressors, inotropes and blood products to reach these goals, with frequent reassessment of these endpoints.[2,3,5] Hyperglycemia is a common occurrence in human PCA patients, and animal studies demonstrate that it worsens ischemic brain injury.[3] Human studies have shown no difference in mortality between PCA patients with tight glycemic control (72-108 mg/dL) versus moderate (108-140 mg/dL) glycemic control.[3] Currently, moderate glycemic control is suggested for human PCA patients, and a similar strategy in dogs and cats may be considered.[2,3] While steroid administration in sepsis and PCA in humans is controversial, CIRCI has been identified in several human clinical studies after ROSC, which has been associated with increased mortality.[3,5] Administration of low-dose hydrocortisone in dogs and cats with vasopressor-dependent shock after CPA, with or without documented CIRCI, is reasonable.[3,5]

Neuroprotective strategies

Mild therapeutic hypothermia (MTH) is recommended in patients that remain comatose after ROSC, if mechanical ventilation and advanced critical care capability is available. MTH helps attenuate further injury to both the brain and heart in PCA. In human medicine, patients are actively cooled to between 89.8 and 92 degrees Fahrenheit core body temperature with cooling blankets, ice packs, IV infusion of ice-cold saline and endovascular cooling devices. It is started immediately after ROSC, but the ideal duration of MTH is unknown, with more severely injured patients likely to require longer duration. MTH is one of the only treatments proven in clinical trials to benefit patients with PCA due to its neuroprotective effects. It decreases mitochondrial injury, reduces cerebral metabolism and decreases production of reactive oxygen species. In dogs and cats, the target MTH is the same as it is for people with slow rewarming (0.25 to 0.5 degrees Celsius per hour) if mechanical ventilation and critical capabilities are possible.[5] These patients must be sedated, intubated and ventilated to avoid shivering and increased muscle tone. However, permissive hypothermia is an alternative in spontaneously hypothermic patients after CPA. The presence of coma absence pupillary light reflex 24 – 72 hours after ROSC significantly increases the likelihood of a poor neurological outcome.

Other neuroprotective strategies include monitoring for non-convulsive seizures (only identified by electroencephalography) and anticonvulsant treatment, as seizures increase cerebral metabolism and oxygen demand.

Myocardial dysfunction

Myocardial injury, and resulting dysfunction, is also likely attenuated by hypothermia. Other than MTH, no other treatments have been identified to be clinically effective in attenuating myocardial dysfunction.[4] Echocardiogram is used for diagnosis and serial echocardiograms for progression, response to treatment and resolution. Dobutamine administration is the treatment of choice for improving systolic function and output in both cats and dogs.[2] Cardiac arrhythmias should also be addressed as needed based on their severity. Fortunately, myocardial dysfunction is reversible and typically resolves in 48 hours.

Reoxygenation

While reoxygenation after global ischemia is the goal of PCA care, controlled reoxygenation is important to avoid both hypoxemia and hyperoxemia. Oxygenation guidelines recommend maintaining a fraction of inspired oxygen (FiO2) that produces an arterial oxygen saturation of 94% – 96%.[5] In the early stages of reperfusion, hyperoxemia harms post-ischemic neurons by causing excessive oxidative stress. Evidence suggests that "arterial hyperoxemia soon after ROSC increases oxidative brain injury and neurodegeneration, and worsens functional neurological outcome and negatively impacts overall survival."[2]

Positive pressure ventilation is not routinely recommended in all PCA patients but is usually needed in the PCA patient that is hypoventilating or is unable to maintain normocapnia or normoxemia.[5]

Precipitating factors

Persistent precipitating pathology and pre-existing comorbidities will influence prognosis, as they will persist after ROSC and add great variability to the PCA patient population. Limited information is available about what these factors are in small-animal populations. Precipitating factors need an individualized approach using critical care principles to support oxygenation, ventilation and circulation to realize a patient's potential for a positive and meaningful outcome.

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How a Raw Food Diet May Affect Patient Care and Outcomes

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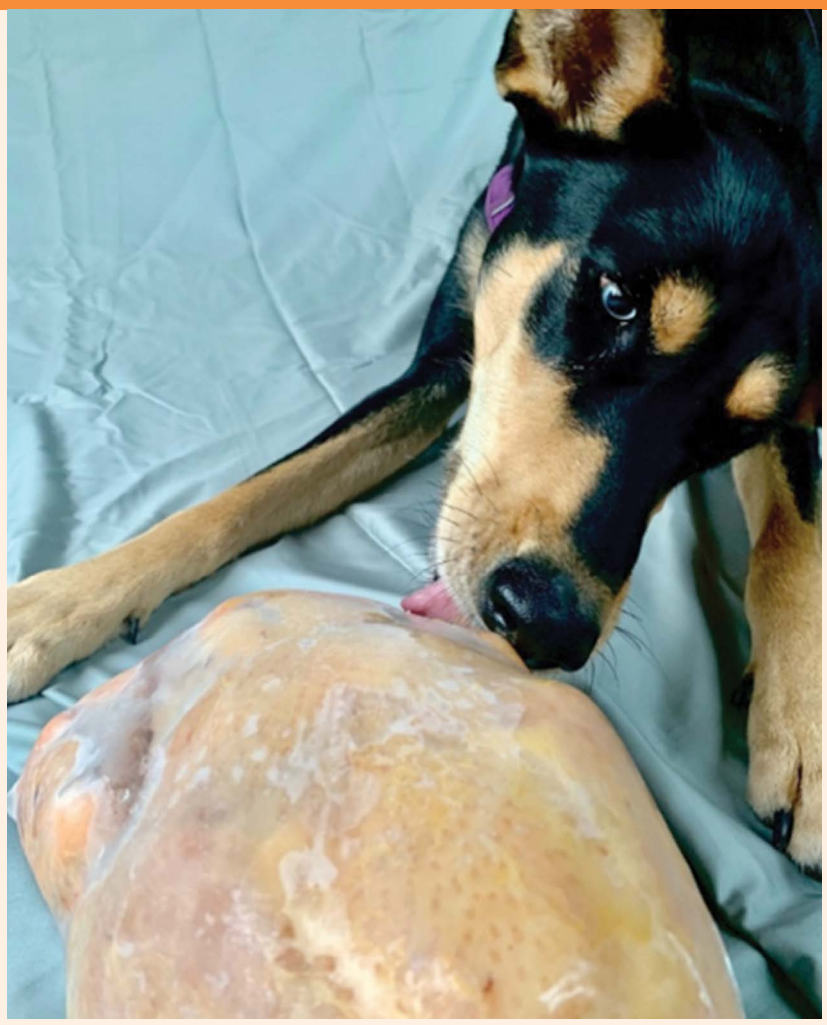
It is well known that recent antibiotic exposure is a risk factor for an animal's infection being more resistant to antibiotics.[1] We routinely ask owners whether a pet has recently been on antibiotics before devising an antibiotic plan for that patient. Newer evidence suggests that there is another equally important risk factor for developing an infection resistant to commonly used antibiotics: feeding a raw-food diet.

The first study linking a raw-food diet to cephalosporin resistance was published in 2008. This group intended to evaluate whether therapy dogs visiting patients in hospitals posed a risk to that vulnerable group of individuals. The group found that the dogs in the therapy program who were fed raw meat within the year of the study were 17 times more likely to shed extended-spectrum cephalosporinase *E. coli* than dogs in the program who were not fed raw diets.[2] Because a common argument from raw-diet proponents is that dogs are exposed to bacteria not through raw diets but treats (such as pig ears), the group controlled for dogs fed such treats and still found that feeding raw was a risk factor. More recently, 580 fecal samples were obtained from dogs in a cross-sectional study of dogs visiting vets in England. Of those samples, multi-drug-resistant *E.coli* were found in 18.3% of samples, and the two risk factors for shedding of resistant organisms were previous antibiotic exposure and being fed a raw diet.[3] In a cohort study of cats, it was found that cats fed a raw diet were 31 times more likely to shed extended-spectrum beta lactamase (ESBL) *Enterobacteriaceae* in their feces.[4] In fact, 89% of cats fed raw diets shed bacteria of this type, which would be resistant not just to amoxicillin-clavulanic acid but also to drugs designed to be resistant to beta lactamase, such as second- and third-generation cephalosporins, which are of critical importance in human medicine.[4] Another study in dogs in the Netherlands showed that dogs fed raw meat were more than twice as likely to shed ESBL *E. coli*.[5] The evidence is now overwhelming that feeding a raw diet increases the antibiotic resistance of enteric flora microbes.



The question remains, however: how does this affect clinical decision-making? Do we know whether having resistant flora in an animal's GI tract leads to an anal sac abscess or a tooth-root abscess being resistant to amoxicillin-clavulanic acid? There are limited case reports that this may occur, and certainly when *Salmonella* is isolated, a link to a raw diet should be investigated.[6] However, studies evaluating whether a raw diet leads to more resistant *infections* (as opposed to more resistant commensal flora) are lacking. What is a clinician to do with this information? I suggest three steps to avoiding treatment failure due to the risk posed by feeding a raw diet:

(CONTINUED ON PAGE 10)

EMERGENCY

How a Raw Food Diet May Affect Patient Care and Outcomes

CONTINUED FROM PAGE 9

1. Ask clients whether they feed a raw diet for every case you see. Note whether the diet is home prepared or commercially prepared and whether it is freeze-dried or high-pressure pasteurized (the latter two methods may reduce some but not all pathogens).

2. If a pet with an infection is fed a raw diet, perform an aerobic culture and educate the owner as to why an aerobic culture is warranted in this case. Make the link for them between raw diets, antibiotic resistance and the potential for treatment failure in this case.

3. In the case of life-threatening infections (e.g., pneumonia, severe soft tissue infections leading to sepsis, abdominal sepsis, hepatic abscesses) when one cannot afford to be wrong in drug selection lest the patient die awaiting culture results, consider a de-escalation approach to antibiotic therapy.

A de-escalation approach to antibiotic therapy requires the clinician to choose drugs that are likely to kill the most resistant pathogens that COULD be causing the infection and then de-escalate to drugs that kill the isolated pathogens based on results of a microbial culture. In the absence of culture results, however, the clinician should de-escalate to a drug that is likely to kill the most COMMON pathogens for the disease process after the animal has recovered to the point when the disease is no longer deemed life-threatening. An example of this approach is to put a dog with signs of systemic inflammatory response syndrome (SIRS) suffering from oxygen-dependent aspiration pneumonia on ampicillin-sulbactam and enrofloxacin, but once the dog is no longer oxygen dependent and is eating and drinking, send the dog home on the oral form of just one of the two drugs. The idea that the animal has to "finish the course" of antibiotics is outdated and based on dogma and not scientific research, so stopping enrofloxacin, for example, after 2 – 3 days of in-hospital therapy is not only reasonable, but also good antimicrobial stewardship.[7]

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*Denotes articles that are Open Access and can be viewed online without a subscription.

↘ MSPCA-Angell Welcomes New President, Neal Litvack

In March 2020, MSPCA-Angell announced that Neal Litvack was hired to serve as our new President. Mr. Litvack stepped into the role on Monday, April 27, replacing Carter Luke, who retired on April 3.

Neal brings an extraordinary background in the for-profit and nonprofit worlds. He is passionate about animals, and about our mission to protect them and advance their health and welfare.

Neal came to us from the American Red Cross, where he served as Chief Marketing Officer. While there, he oversaw all marketing, including brand development and stewardship. He previously served as Chief Development Officer, raising $630 million annually and $2.7 billion in additional funds for major disasters.

Prior to his work at the Red Cross, he held executive-level roles spanning marketing, finance and operations at renowned institutions and companies, including Milton Academy, Fidelity Investments, and HBO.

Neal's involvement in the humane world includes serving on the board of PetSmart Charities, which is committed to finding lifelong homes for all pets by supporting programs and thought leadership that bring people and pets together. And he was previously a board member at the Animal Rescue League of Boston, and at Buddy Dog Humane Society.

Let Them Heal: Dog-Training Fun Before and After Rehab

Terri Bright, PhD, BCBA-D, CAAB

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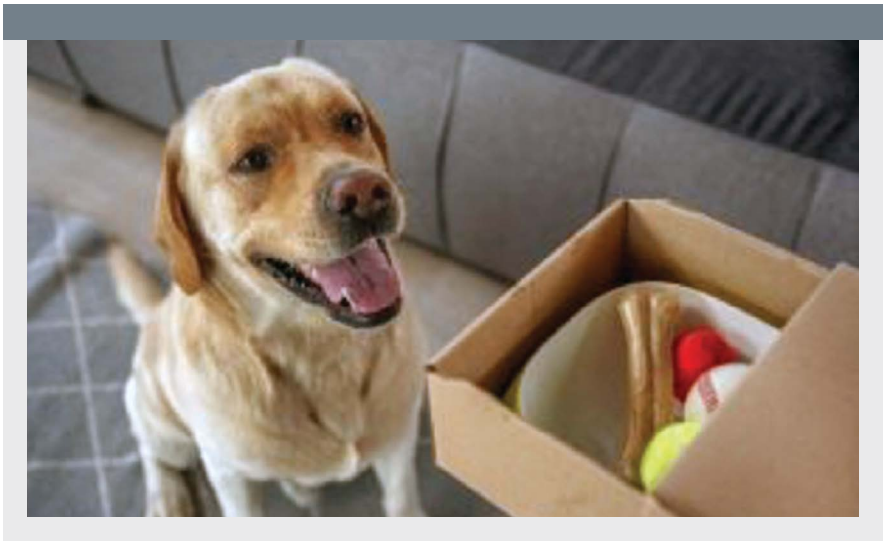
The social ability of dogs has typically allowed them to access their favorite activities at their whim: Throw the ball! Chase me! Take me for a 5-mile walk! As they have throughout 10,000 – 30,000 years of co-evolution, owners comply. When the owner discovers that the dog needs prolonged rest or surgery that will require long periods of forced inactivity, they are dismayed to say the least. Language cannot convey to the dog the importance of this period of massive sea change; we can't say, "This is only for six weeks, I promise!" Instead, the dog's behavior must be carefully shaped to achieve the best therapeutic outcome.



WHAT AND WHEN TO TRAIN

The best time to train keep-your-dog-quiet-type behaviors is before they are needed. The young puppy or new adult dog can easily be taught behaviors that will hold them in good stead throughout their lives, during vet visits and as needed for all other necessary handling and injury- or illness-induced rest. These behaviors can be separated into two classifications: "foundation" behaviors, which will be used daily throughout the dog's life; and "cusp" behaviors, which can be built upon to achieve other behaviors. If you have a patient with a known surgical prognosis, you cannot guide the patient to training too soon.

FOUNDATION BEHAVIOR AND HOW TO TRAIN

These should be part of the curriculum of any typical obedience class: sit, down-stay, come when called, and loose-leash walking. Ideally, they are taught without the use of force and with lots of rewards, such as food treats, toys, play and owner attention. The clicker can be a handy tool once paired with food; however, results can just as easily be obtained with a word as a marker; the clicker and/or the word should tell the dog that food, praise or a toy is coming because of what you just did! Any method that uses something to force or frighten the dog, such as prongs or electronic collars, can have unwanted side effects, such as avoiding the trainer/owner, fear of environmental stimuli or aggression. Even staring at, pointing or yelling can frighten dogs, and given the state of many "rescued" dogs, such as being under-socialized or even feral, confidence needs to be built upon, not shredded. To avoid these side effects, which could tremendously affect the injured or surgicalized dog, the modern veterinarian refers only to trainers who do not use force. This can be ascertained with one simple question: "Do you need any special equipment to train?"

CUSP BEHAVIORS

Cusp behaviors are used to build other moving or stationary behaviors. Training to "target" (touch) or move toward a hand or an object is universally used in aquariums and zoos, where one cannot use a leash. "Station" training has the same advantage, as it teaches the animal to "Stay on this place." Crate training carries an obvious advantage for dogs, and all owners should be encouraged to teach this to their puppies or dogs. (Note that it can be difficult for dogs that have been transported in a crate without being trained to its use and were thus traumatized.) Training a dog to walk up a ramp is another cusp skill that can be used early on in a sport, such as agility, or for the oldster getting into the car. Again, teaching a young puppy or dog this skill can save much trauma in future years, as elderly dogs in pain may not be as eager to learn this skill. The "head-hold" is another great skill for any dog: simply reward the dog for resting its head on your open palm. For blood draws or medicating, this is a terrific skill; along these same lines, teaching a dog to "settle" on its side can be the difference between war and peace in the veterinary visit.

ENVIRONMENTAL CONTROL AND ENRICHMENT

The owner of the injured dog or one under post-surgical care should arrange the environment such that behavior is controlled. All family members and caretakers (e.g., dog walkers) must be on the same page in regard to training and control of the dog during its "down" time; otherwise, optimum healing results may not be achieved. The dog's behavior should be managed as if the dog were a two-year-old child; every action should be arranged, then supervised, to enhance healing. Baby gates, ex-pens, a crate, stairs to couches and beds, and supervision during all transitions will be necessary. Inexpensive toys can be stockpiled and delivered as needed; their destruction should

(CONTINUED ON PAGE 12)

BEHAVIOR

Let Them Heal: Dog-Training Fun Before and After Rehab

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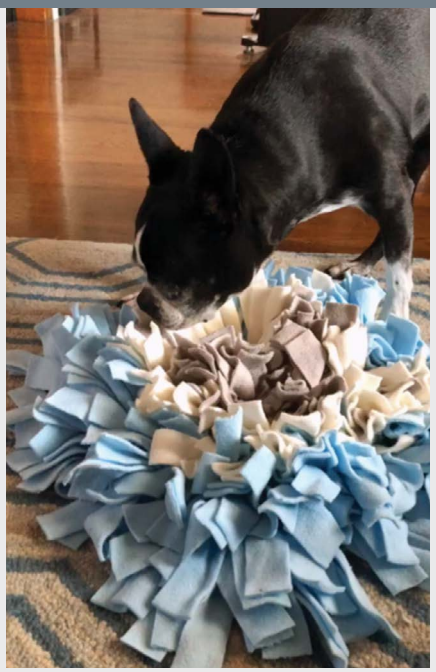


be expected, but the owner should avoid things he or she knows the dog will ingest. Food-delivery toys should be used for all meals. Helpful equipment includes:

- "Snuffle" mat: has inches-deep fibers into which the owner puts kibble for the dog to sniff out/eat.
- "Treat and Train": a machine that delivers food remotely, first at the push of a button and then automatically. Invented by Dr. Sophia Yin, it comes with clear instructions, the final result of which is a dog on a down-stay that it will hold until the food runs out (which can be scheduled for quite long periods of time).
- "Lick" mat: plastic mats onto which one can smear peanut butter or wet food for the dog to lick; some come with suction cups so they can be stuck onto a cabinet or the side of a bathtub.
- "Pupcake": a homemade treat. Fill a cake pan with water; add some meat broth; add a handful of kibble; grate some cheese on the top; and freeze.
- Anything in a Kong: we like to use the Stella and Chewy freeze-dried patties: cut off one-third of the patty; squish the Kong so that you can barely slide the patty in. The patty-lover will lick and bounce the Kong for a long time to get the food out.
- Kong Wobbler: a hard-plastic toy the dog knocks around and from which it gets food.
- Tricky Treat ball or Snoop: soft versions of moving toys out of which to get food.

NOSEWORK

A dog is basically a nose on legs, and every dog should have deliberate scent-based enrichment added to its routine. For the dog on restricted activity, it is a godsend. You can keep it as simple as tossing a handful of kibble into the grass for the dog to find, hiding a treat under one of three cups for a Monty game, or exploring the competitive skill of finding discrete scents a la bomb-sniffing K9s. (We have many nosework classes at the MSPCA.) It is truly the most bang for your enrichment buck.

ALTERNATIVE BEHAVIORS CAN BE TAUGHT

Giving the owners something to do with their dogs instead of just saying "Don't let the dog _____" can result in new and useful behaviors and a better-trained dog. Instead of jumping or running, owners can use the follow-my-finger game to teach the dog to heel at their left side in a circle. By the time the dog's injury is healed, the dog will be a great heeler. Another trained behavior taken from the obedience ring is "come front": the owner's backward step is a cue to the dog to turn, sit and give the owner attention. For example, since roughhousing cannot be allowed, all of the above enrichment activities can replace overzealous playing that, even during non-injured times, can get out of hand. "Touch" games and tricks can replace out-of-control behavior. Food toys can be used to placate the cone-wearing dog and give it other things to lick. If the dog is a chronic puller, a harness, such as the Freedom No-Pull harness, can be used for walking. With the above interventions, the healing dog can become the healthier, better-trained and easy-to-live-with family companion.

Note: RehOB (Rehab/Obedience) and Low-Impact Agility are both taught at Angell West: angell.org/dogtraining

Terri Bright, PhD, BCBA-D, CAAB

↘ Angell Offers Behavior Teleconsult Appointments

These are challenging times for all of us, but Angell is here to help. Dr. Terri Bright and the Behavior team can assist with pet behavior problems via teleconsult appointments. At the time of this writing, our Behavior service is not yet seeing patients in person.

If a dog has separation anxiety, there is no time like the present to teach them to cope with being alone. Dr. Bright and her team can also help with new puppy behavior. Even many aggression cases can be conducted by phone or video chat.

The integrity of our expertise is upheld at all times and if we feel we can't assess a case remotely, we will provide stopgap management guidelines for the client until they can be seen personally.

Simply have your client call our Behavior office at **617-989-1520** or visit **angell.org/behavior** for more information.

↘ Angell Now Offers Two Low-Cost Clinic Locations

Angell at Essex (Danvers, MA) and Angell at Nashoba (Westford, MA) clinics are dedicated to providing quality care to the general public as well as offering deeply discounted services for qualified low-income families. The clinics provide primary veterinary care, spay and neuter services, vaccinations, and surgery and dental services.

Angell at Essex and Angell at Nashoba are open weekdays from 7:45am – 4:00pm throughout the year. The clinics do not provide overnight care, specialty service care, or 24/7 emergency care. Appropriate cases will be referred to Angell's Boston or Waltham facilities or a surrounding specialty veterinary referral hospital.

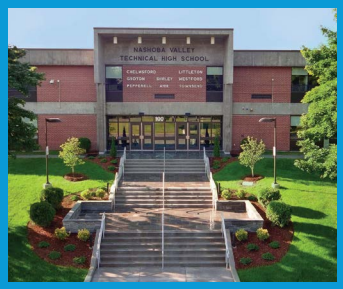
To Financially Qualify for Discounted Services

Angell clinics welcome all pet owners and reserve a sizable portion of appointment times for discounted services. For those interested in discounted services, clients must financially qualify by presenting a photo ID and one of the following:

- Women, Infants, and Children (WIC) Program card
- Supplemental Nutrition Assistance Program (SNAP) card (formerly known as Food Stamps/EBT)
- Spay and Neuter Assistance Program certificate
- Letter/lease from the owner's local housing authority showing that the owner is a participant in public housing
- Veterans card

angell at nashoba

To schedule an appointment with the Angell at Nashoba clinic, please call **978-577-5992**.



Left to Right: Dr. Laurence Sawyer. Angell at Nashoba on campus at Nashoba Valley Technical High School (Westford, MA).

angell at essex

To schedule an appointment with the Angell at Essex clinic, please call **978-304-4648**.

Left to Right: Dr. Erin Turowski. Angell at Essex on campus at Essex North Shore Agricultural and Technical School (Danvers, MA).

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(W/B) Services also available at our Waltham location

↘ Our Service Locations

BOSTON & WALTHAM	BOSTON ONLY
Avian & Exotic Medicine 617-989-1561	**Anesthesiology** 617-541-5048
Behavior 617-989-1520	**Dentistry** 617-522-7282
Cardiology 617-541-5038	**Diagnostic Imaging** 617-541-5139
Dermatology 617-524-5733	**Oncology** 617-541-5136
Internal Medicine 617-541-5186	**Ophthalmology** 617-541-5095
Neurology 617-541-5140	**Pathology*** 614-541-5014
Physical Rehabilitation** 781-902-8400	
Surgery 617-541-5048	

24/7 Emergency & Critical Care ■ Boston: 617-522-5011 ■ Waltham: 781-902-8400

*Boston-based pathologists serve both Boston and Waltham locations **Available only in Waltham

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Please consider adding Angell's main numbers to your after-hours phone message.

↘ Courtesy Shuttle for Patients Needing Further Specialized Care

Angell Animal Medical Center offers the convenience of our MSPCA-Angell West facility in Waltham, MA. With 24/7 Emergency and Critical Care service and two board-certified criticalists on staff, the Waltham facility also offers specialized service appointments Monday through Saturday. If needed, an oxygen-equipped courtesy shuttle can transport animals to Boston for further specialized care and then take them back to Waltham. Whether in Boston or in Waltham, our specialists regularly collaborate and plan treatments tailored to our patients' emergency, surgical, and specialty needs.

WE OFFER A BROAD RANGE OF EXPERTISE AND DELIVER THIS CARE WITH THE ONE-ON-ONE COMPASSION THAT OUR CLIENTS AND PATIENTS DESERVE.