



# Partners In Care

Veterinary Referral News from Angell Animal Medical Center

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## ANESTHESIA



### Prehospital Sedation of Cats

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**I**mproving the feline experience at the time of the veterinary visit and time surrounding that visit is imperative in cats. Cats, however, can be a far more challenging species to judge behaviorally as they are often less interactive and more elusive than dogs. In stressful situations, such as the unexpected car ride or annual exam, the fearful and anxious cat may display aggressive behaviors such as biting and swatting, which can cause self-trauma, harm to the owner, and/or harm to the veterinary staff. The therapies included in this brief article are meant to reduce anxiety and arousal in cats, with the goal of enhancing the entire veterinary visit experience for all involved. The author encourages the use of the included pharmacologic interventions IN TANDEM with other practices such as dedicated cat-friendly environments and “Fear-Free” handling techniques (e.g., body wraps, feline pheromones, etc.). Whenever possible, a full physical exam should be done before prescribing prehospital sedatives.

**Gabapentin** binds to calcium  $\alpha 2$ - $\delta$  receptors in the dorsal horn of the spinal cord and forebrain, having an inhibitory effect.<sup>1,2,3,4</sup> It has long-term historical use as an adjunctive analgesic in both humans and animals;<sup>1,4,5</sup> however, its antiepileptic properties are likely responsible for sedation. In the acute setting, sedation following gabapentin administration is often profound. This was

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## CARDIOLOGY



### Endovascular Stents

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**I**nterventional Radiology (IR) is a growing field in veterinary medicine, with rapid advancements allowing for alternate treatment protocols and improved patient care. Various disease conditions are now being diagnosed and treated via IR techniques. These include congenital and acquired cardiac diseases (e.g., transarterial occlusion of patent ductus arteriosus, transvenous pacemaker implantation), urologic conditions such as urethral stenting for obstructive tumors, nasopharyngeal and tracheal diseases, and targeted oncologic treatments, such as intraarterial chemotherapy delivery. These techniques may allow for less-invasive options and potentially faster recovery times. Two such conditions that are now being managed with the use of endovascular stents include intrahepatic portosystemic shunts (IHPSS) and extraluminal compression secondary to cardiac tumors.

#### PERCUTANEOUS TRANSVENOUS EMBOLIZATION FOR IHPSS

Portosystemic shunts (PSS) are vascular anomalies in which there is a connection between the portal and systemic venous system, thus bypassing the liver causing hepatic dysfunction, gastrointestinal (GI) disease, including GI ulceration, and clinical symptoms such as hepatic encephalopathy. Congenital IHPSS account for about 25-33% of all congenital PSSs in dogs and cats; IHPSS are more common in medium- to large-breed dogs.<sup>1,2</sup>

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Table 1: Dosing and timeline of administration for sedative agents. Timing regimen should be adjusted based on cat's appointment time.

| DRUG         | DOSE   | WHEN TO ADMINISTER*   | CONTRAINDICATIONS  |
|--------------|--|---|--|
| Acepromazine | <b>Recommended:</b><br>Injectable (OTM):<br>0.01-0.05 mg/kg<br>Small volumes<br>can be diluted<br>with 0.9%<br>saline for easier<br>administration | Time of onset ~30<br>minutes, so best given<br>30-60 minutes before<br>hospital visit   | <ul style="list-style-type: none"> <li>• Undiagnosed heart murmur, known heart disease</li> <li>• Trauma patients</li> <li>• Critically ill</li> <li>• Kidney disease</li> <li>• Liver failure</li> <li>• Pediatrics and geriatrics</li> </ul> |
| Gabapentin   | 15-30 mg/kg<br>For most<br>average cats,<br>100 mg capsule<br>recommended  | Give PO the night prior to<br>hospital visit, then repeat<br>same dose the morning of<br>hospital visit (at least two<br>hours prior) | <ul style="list-style-type: none"> <li>• Liver failure</li> <li>• Pediatrics</li> </ul>  |
| Trazodone    | 5-10 mg/kg<br>For most<br>average cats,<br>50 mg tablet<br>recommended   | Give PO the night prior to<br>hospital visit, then repeat<br>same dose the morning of<br>hospital visit (at least two<br>hours prior) | <ul style="list-style-type: none"> <li>• Preexisting arrhythmias</li> <li>• Patients on monoamine oxidase inhibitors (MOAIs)</li> </ul>  |

highlighted in a recent study in which both owners and veterinarians observed stress reduction, improved compliance, and less aggression in cats that received gabapentin 90 minutes prior to transport to the veterinary hospital.<sup>6</sup> Owners need to be made aware that their pet will often appear considerably more sedate at home. Cats should be more closely supervised on stairs or when jumping place to place, given ataxia that may occur following administration. Dosing recommendations and timelines are proposed in Table 1.<sup>6</sup> Gabapentin is an ideal agent to use alone, especially in those cats that may be older and have more chronic pain states, as the drug provides sedation and analgesia without undesirable adverse effects.<sup>4,5,6</sup> It can be used in combination with the other included agents in cats needing additional sedation.

**Trazodone** is classified as a serotonin receptor antagonist and reuptake inhibitor (SARI),<sup>1,7,8</sup> with historical use in anxious dogs. Two recent studies in two different feline populations – 1.) a research setting<sup>7</sup> and 2.) client-owned cats in the clinical setting<sup>8</sup> – indicated that trazodone was well tolerated and resulted in cats with improved behavior and tractability scores. Of note in the clinical study was that owners, too, observed key behavioral improvements following trazodone administration in comparison to a placebo.<sup>8</sup> In laboratory cats, trazodone caused no remarkable changes to physical exam and/or laboratory values,<sup>7</sup> adding to its margin of safety in older, potentially debilitated patients. Pharmacokinetic data have not been measured, but studies indicate peak sedation within 1-3 hours after dosing (Table 1).

**Acepromazine** is part of the phenothiazine class of sedatives and has widespread use within the veterinary world, primarily during the perianesthetic period. Acepromazine elicits behavior-modifying effects primarily by drug binding and blockade of dopamine receptors in the basal ganglia and limbic system.<sup>1,2</sup> The drug exists for veterinary use in two forms – oral and injectable. The injectable form, when administered oral transmucosally (OTM), offers very reliable moderate to marked sedation in cats within 20 to 30 minutes. With this route of administration, the dose closely follows recommended intramuscular (IM) dosing (Table 1).<sup>1,2,4</sup> In the aggressive or fearful cat, this drug is best given 30-60 minutes prior to the hospital visit with administration guidelines similar to OTM buprenorphine (effects are most profound

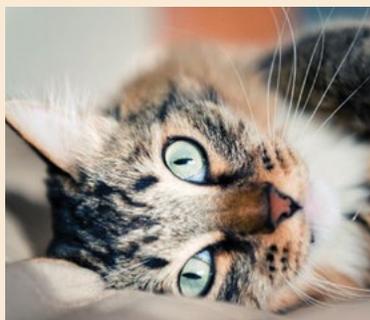
following absorption from the oral mucosa). Given a higher prevalence of heart disease in cats, acepromazine should be avoided in any cat with a heart murmur of unknown origin and cats with known hypertrophic cardiomyopathy (HCM) as safer alternatives exist and the effects of acepromazine are NOT reversible. Other contraindications include disease states that would deter one from using acepromazine in an anesthetic protocol.

In considering what pharmacologic intervention to start with, it is recommended to move in a stepwise process. Gabapentin and trazodone are recommended as first-line choices in ameliorating feline anxiety and aggression, as they have both been shown to be safe and effective options to improve feline veterinary visits. They can be given independently (start with one, as you can always add more if needed) or together in those cats requiring increased sedation. All of these oral therapies can be combined with standard anesthetic protocols; however, when using acepromazine OTM, any additional doses of injectable acepromazine should be dose-reduced. As a final reminder, all of these therapies should be combined with cat-friendly practices and low-stress handling techniques.

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Whenever possible, a full physical exam should be done before prescribing prehospital sedative.



Continued from page 2

Traditional surgical approaches for treatment of IHPSS have been associated with relatively high perioperative complication and mortality rates. Endovascular attenuation has recently been described, which can allow for similar results and fewer perioperative complications compared to those reported following standard surgical approaches. Percutaneous transvenous embolization (PTE) requires placement of a stent within the caudal vena cava followed by deployment of multiple coils, allowing for slow reduction of the shunt.<sup>3</sup>

Medical management is initiated at time of diagnosis of IHPSS, and dogs are allowed time to grow to near-adult body size prior to PTE. A CT angiography (CTA) or MRI is obtained prior to the procedure to allow for evaluation of the patient's anatomy and to estimate which size stent will be needed. The procedure is performed under general anesthesia. A large introducer catheter is placed percutaneously into the right jugular vein, allowing for passage of various catheters and

wires into the IHPSS and portal vein. Portal pressure and caval pressure measurements are obtained throughout the procedure in order to help guide the treatment plan and to avoid portal hypertension. Ultimately, a stent is advanced and deployed within the caudal vena cava using fluoroscopic guidance, ensuring that the entire entrance of the shunt is spanned by the stent. Thrombogenic stainless steel coils are then delivered into the shunt at the junction of the stent and hepatic vein; the stent prevents the coils from migrating into the caudal vena cava. (Figure 1). Coils are added while monitoring portal pressures until the shunt pressures are within the desired range, indicating appropriate attenuation of the shunt.<sup>3,4</sup>

Favorable outcomes for PTE have been reported in the literature. When performed by someone with experience in IR procedures, outcomes are fair to excellent in 81% of patients (15% fair, 66% excellent) with a mean survival time over six years and <5% perioperative mortality rate. This

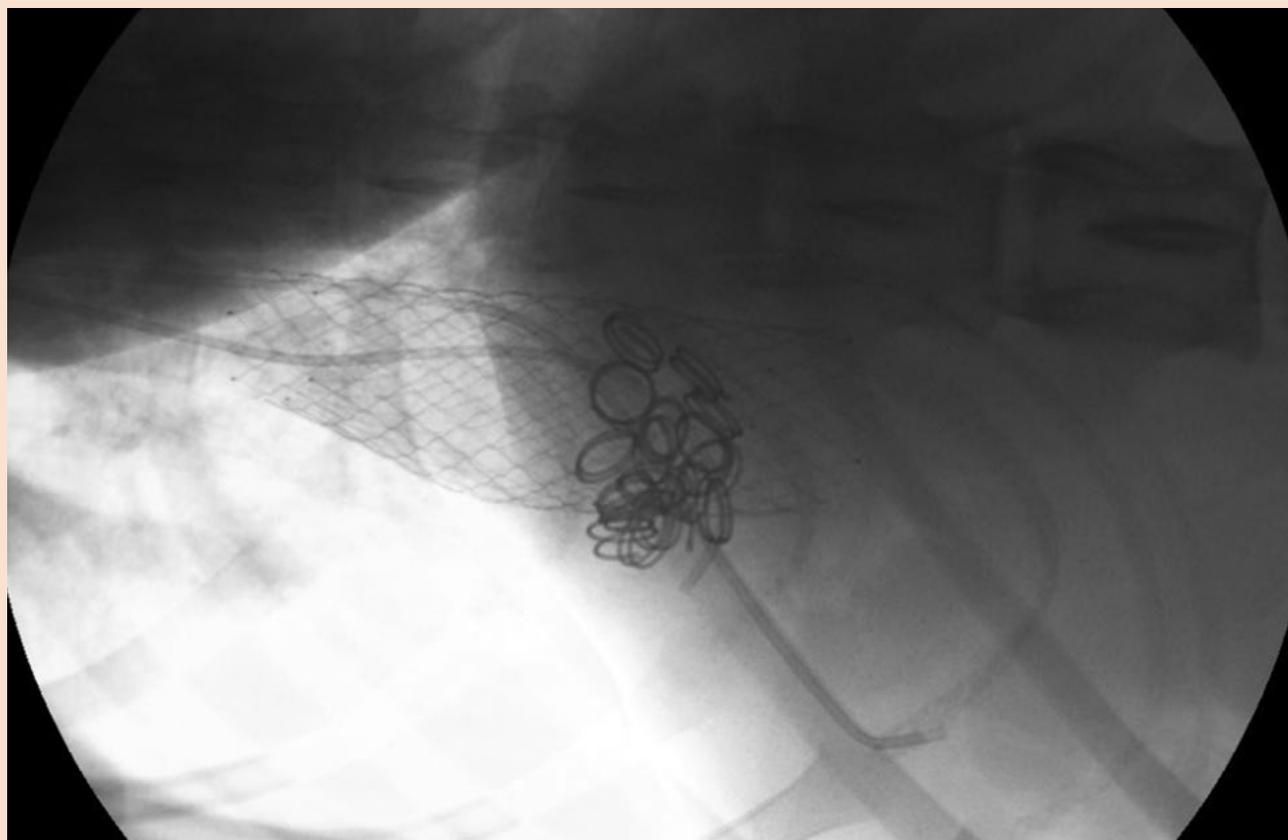
treatment option should be considered in patients with IHPSS.<sup>3,4</sup>

#### PALLIATION FOR CARDIAC-ASSOCIATED TUMORS

Endovascular stents are also being used for palliation of extraluminal obstruction from cardiac-associated tumors. Right atrial/auricular or heart-based tumors such as chemodectomas can result in right atrial or pulmonary artery compression and/or caval obstruction causing decreased venous return to the heart (Budd-Chiari-like syndrome). Physical exam findings or clinical abnormalities that can be associated with venous obstruction include jugular distension, edema of the head and neck, tachypnea, pleural effusion, ascites, arrhythmias, etc. Medical management and paracenteses may help alleviate some of these symptoms, though typically only for the short term. Additional treatments, including surgical options (pericardiectomy or pericardial window), radiation therapy, or chemotherapy, can be performed in patients with

FIGURE 1

↘ Intraoperative fluoroscopy image obtained from a canine with IHPSS. Caval stent is in place, and multiple thrombogenic coils have been deployed.



these types of tumors. Intervention via caval or pulmonary artery stenting may alleviate the previously described clinical signs.<sup>5,6</sup>

A thorough diagnostic workup and consultation with a cardiologist, oncologist, surgeon, and/or radiologist should occur prior to proceeding with intervention. Ideally, a CTA or MRI with angiography should be performed to detail the extent and anatomy of obstructions, as well as provide measurements for appropriate stent sizing and to ensure all equipment is available. Surgical approach for these procedures will depend on the location of the obstruction and stent deployment, though most commonly would involve a transvenous approach via the jugular or femoral vein. Typically, self-expanding metallic stents are used.<sup>5</sup>

Stent placement for these types of conditions has been reported in the literature. In a case report of three dogs with right atrial masses causing obstruction to venous return, transatrial stents were successfully deployed. Two dogs required additional stent placement due to stent occlusion. Survival times ranged from 5.5 months up to 22 months following initial stent placement.<sup>5</sup> Another case series described successful caudal vena cava and/or hepatic vein stent placement for treatment of three dogs with diminished venous blood flow from obstructive neoplasms.<sup>7</sup> Lastly, another case series described successful cranial vena cava and branch pulmonary artery stenting in two dogs with chylothorax secondary to increased cranial cava pressure from obstructive cardiac masses.<sup>8</sup> Postoperative survival times for the dogs of the latter two case series ranged from six to 20 months. All cases reported were considered successful with

initial alleviation of clinical signs associated with obstructive cardiac masses.

#### ADVANTAGES AND POTENTIAL COMPLICATIONS

Endovascular stent placement can provide alternative treatment or palliative options for patients with a variety of conditions, including IHPSS and extraluminal compression from obstructive cardiac-associated masses. Potential benefits of minimally invasive IR or interventional cardiology procedures compared to traditional options often include shortened anesthesia time, smaller incisions allowing for decreased pain and more rapid recovery times, and alleviating clinical signs associated with conditions for which alternate treatment options may not be available. Complications associated with endovascular stent placement are likely to be minor. These could include hemorrhage from the vascular access site, thrombus formation due to turbulence through the stent or defects of the stent, and intraoperative arrhythmias. More significant complications can include stent fracture or migration. With progression of the disease process over time, there is also the potential for obstruction of the stent, causing recurrence of clinical signs and the need for further stenting to alleviate these signs.<sup>5-8</sup>

There are a variety of diseases that are now being managed via interventional and minimally invasive approaches. With the currently expanding Interventional Radiology program at Angell, we seek to continue to offer definitive and palliative treatment options for conditions that either were previously considered untreatable or to provide innovative treatment options alongside traditional therapies.

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## ▾ PHYSICAL REHABILITATION NOW AVAILABLE AT MSPCA-ANGELL WEST

Canine physical rehabilitation is used to treat a wide variety of orthopedic and neurological conditions. Whether recovering from an injury, cross training, or facing mobility issues, dogs can substantially benefit from physical rehabilitation.

With the addition of Dr. Palmer and Dr. Straut, MSPCA-Angell West Physical Rehabilitation has expanded its hours and offers services seven days per week. Dr. Jennifer Palmer earned her DVM from the University of Wisconsin, School of Veterinary Medicine and became a Certified Canine Rehabilitation Therapist (CCRT) through the Canine Rehabilitation Institute. Dr. Amy Straut earned her DVM from the Tufts Cummings School of Veterinary Medicine and became a CCRT through the Canine Rehabilitation Institute.

*Current physical rehabilitation services include:*

 HYDROTHERAPY

 THERAPEUTIC LASER

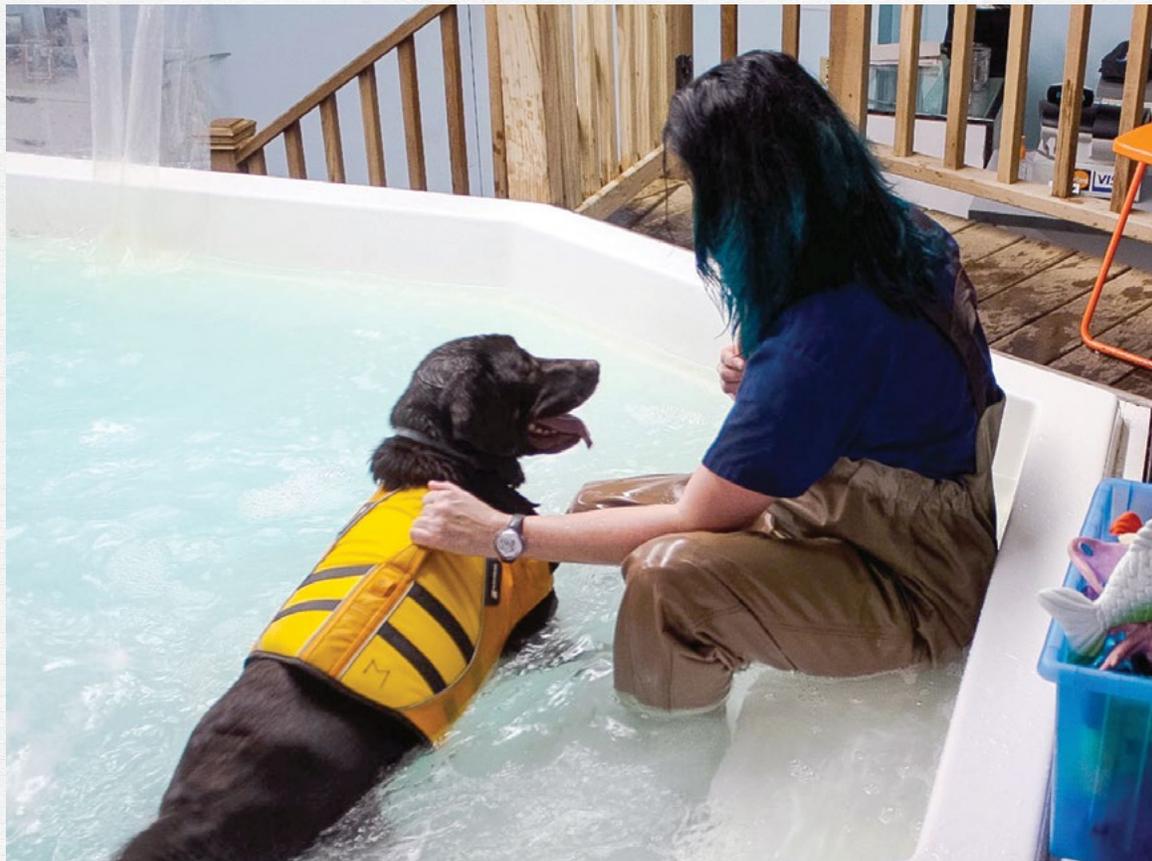
 CONSULTATION AND FITTING OF ASSISTIVE DEVICES

 LAND-BASED EXERCISE

 MASSAGE

 ACUPUNCTURE

 MANUAL THERAPY





## A Novel Local Anesthetic: Nocita<sup>®</sup> (bupivacaine liposome injectable solution)

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**P**eroperative analgesia has become recognized as one of the most important parts of providing superior care for dogs and cats before and after surgical procedures. The mainstays of perioperative analgesia include opioids, alpha-2 agonists, ketamine, NSAIDs, and local anesthetics. Each of these drug classes, while providing pain relief, also present their own unique side effects and affect each patient differently. Opioids, for example, are the most commonly used analgesic drugs in veterinary medicine due to their superior safety profile and excellent analgesic properties, but are fraught with adverse effects such as dysphoria, vomiting, ileus, nausea, and regurgitation. Local anesthetic drugs, such as bupivacaine and lidocaine, are unique in that they can be used locoregionally instead of systemically, thereby providing analgesia while minimizing side effects. Local anesthetics work by blocking sodium channels along nerves, inhibiting excitation and blocking conduction and nerve transmission. Local anesthetics have both a peripheral effect on the nociceptors at the site of injury as well as a central effect in the spinal cord. They not only act on nociceptors (pain receptors) but also on vascular smooth muscle, nerves, and the heart. Local anesthetics can be administered via several routes, including topical application, spinal anesthesia, epidural injection, intravenous infusion, and regionally by nerve blocks. Many consider local anesthetics to be the only true analgesic due to the fact that they provide preemptive analgesia by actually blocking pain transmission versus the treatment of pain after it occurs.

Recently NOCITA, bupivacaine liposome injectable suspension, was introduced into the veterinary market by Aratana Therapeutics. This novel therapeutic is approved for use in dogs undergoing stifle surgery and intended to provide 72 hours of postoperative pain relief. It is labeled for single-dose administration and use within four hours. NOCITA acts by releasing the local anesthetic bupivacaine slowly over 72 hours from the injection site. The liposomal technology, named DepoFoam<sup>®</sup> bupivacaine, has been used with much success in human medicine since 2011.<sup>1</sup> DepoFoam technology involves multivesicular liposomes that encapsulate aqueous bupivacaine. The liposomes are made up of nonconcentric lipid bilayers and, as these bilayers are broken down by enzymes, the bupivacaine is gradually released over 72 hours (Figure 1).<sup>2</sup> During the FDA approval of DepoFoam, liposomal bupivacaine was extensively studied in dogs and was found to be well tolerated and have an acceptable safety profile.<sup>3,4</sup>

NOCITA is administered by the surgeon at the site of surgery using the moving needle technique (Figure 2).<sup>5</sup> Once the bupivacaine is released from the liposome after the lipid bilayers are broken down, its pharmacokinetics and pharmacodynamics are expected to be similar to bupivacaine HCL.<sup>6</sup> Bupivacaine elimination depends largely on binding to plasma proteins in systemic circulation and hepatic metabolism. Excretion of bupivacaine is mainly performed by the kidneys. In patients with marked hepatic disease or dysfunction, NOCITA should be used with caution as they may be more prone to toxicities of local anesthetics such as seizures, tremors, or circulatory collapse. Many surgeons worry about delayed wound healing with local

FIGURE 1

Microscopic structure of a liposome. | [https://www.researchgate.net/figure/Cross-sectional-diagram-of-DepoFoam-containing-bupivacaine-Image-supplied-courtesy-of\\_232226382](https://www.researchgate.net/figure/Cross-sectional-diagram-of-DepoFoam-containing-bupivacaine-Image-supplied-courtesy-of_232226382)

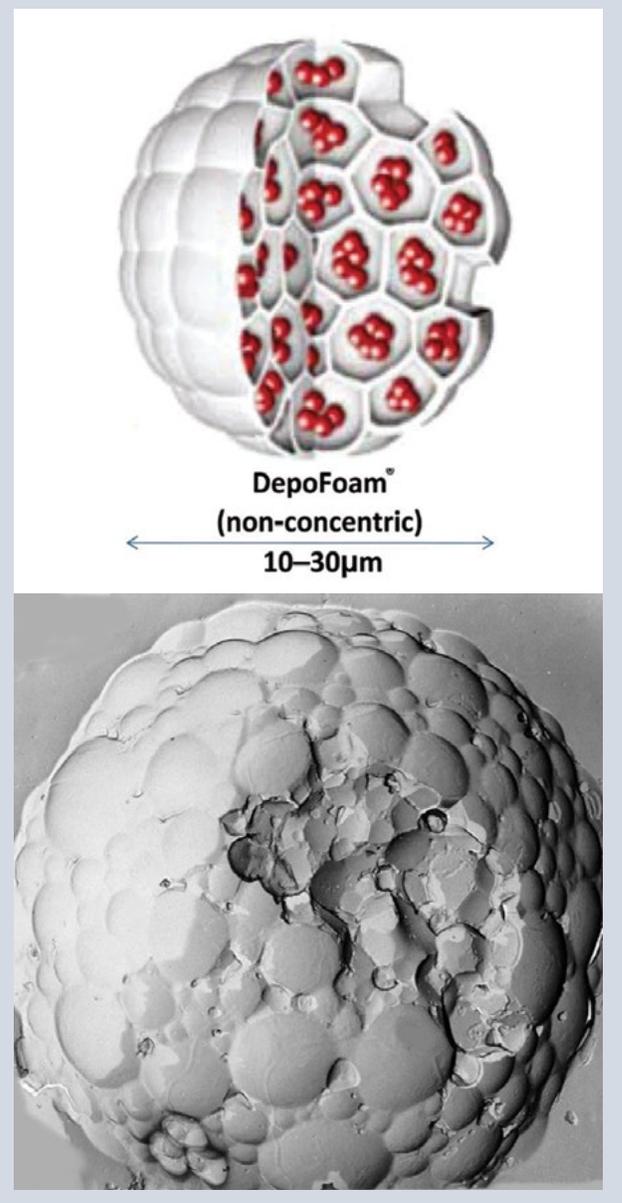
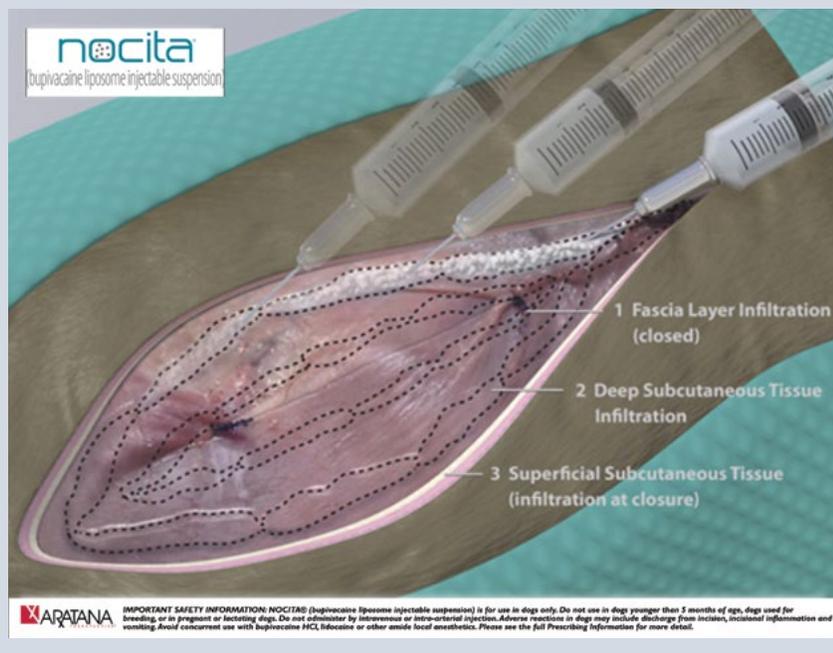


FIGURE 2

↘ The moving needle technique | <http://nocita.aratana.com/dosingandadministration-2>



anesthetics, but studies have shown this not to be a problem with the use of NOCITA.<sup>7</sup> Another study showed that local irritation or tissue damage was mild with the use of liposomal bupivacaine, but that swollen or thickened injection sites can be seen.<sup>8</sup> Overall, it seems that the adverse effects noted with the use of NOCITA are minimal in comparison to the excellent analgesia provided by the drug.

Although at this time NOCITA is approved only for use in dogs undergoing stifle surgery, it is also used off label in both dogs and cats. NOCITA is prescribed for use in procedures associated with severe post-operative pain such as thoracotomies or amputations. Prior to the use of NOCITA in these procedures, diffusion catheters were placed at the surgical site, allowing infusion of a local anesthetic to provide postoperative analgesia for 24 hours. Adverse effects of diffusion catheters included seroma formation, irritation at the catheter site, infection at the site, or accidental intravascular injection. The use of NOCITA avoids the need for a diffusion catheter at the surgical site, also avoiding the adverse effects noted with diffusion catheter use. Subjectively, patients receiving NOCITA have seemed very comfortable and have required fewer systemic analgesics. It is of the author's opinion that these patients also seem to eat sooner after the procedure and are more mobile than the patients

prior to the use of NOCITA. Other procedures in which NOCITA can be used off label include mastectomies, mass removals, or fracture repairs in both dogs and cats.

The introduction of NOCITA into the veterinary market has allowed us to greatly improve how we provide postoperative analgesia to our patients. Unlike locoregional anesthesia techniques, including epidurals or peripheral nerve blocks, the proper use of NOCITA can be easily learned and used by all practitioners. Although expensive, the benefits of adding NOCITA to a practice's arsenal of available analgesic drugs will greatly outweigh the costs when it comes to patient comfort and client satisfaction. Hopefully, in the future, the label use of NOCITA will be expanded for use in both dogs and cats and in many different surgical procedures.

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## Approach to Respiratory Disease in Backyard Chickens

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In recent years, the popularity of backyard chickens has grown considerably. Zoning legislation has created a platform for urban and suburban homeowners to legally invest in small flocks. The average home has fewer than 10 birds, and most cite egg consumption to be the primary purpose, while pet ownership is a close second. In a recent USDA survey, less than half of flock owners were aware of common health concerns that could affect their flock. Respiratory diseases, while often not life-threatening, are one of the most commonly observed ailments by owners. Prevention and risk reduction are critical components for maintaining respiratory health, but recognizing symptoms is also important in guiding treatment.

Appropriate housing plays a large role in reducing the risk of respiratory infections. Whether you are converting an existing shed or purchasing a ready-made coop, it is important to determine the degree of ventilation it provides. During summer months, windows can be opened to improve air quality and air exchange. Birds that have access to a run are also exposed to fresh air. The frequency of respiratory infections increases during the fall when it's cool at night but warm during the day. When the coop isn't reopened in the morning prior to increasing temperatures, a humidity spike will take a toll on the confined flock's respiratory tract. A common misconception is that a coop needs to be airtight to improve heat trapping. In actuality, cracks at the seams along the rooflines allow for a limited exchange of cool air coming in, warming up, absorbing moisture, and then exhausting out of the coop again. Chickens are very efficient at staying warm – as long as they are not in direct exposure to a draft. For this reason, windows don't always allow for the best winter air exchange. If ventilation is lacking, the humidity created by the chickens and their feces will build up on the walls and windows. An ammonia level higher than 25ppm is enough to damage cilia in the airways of chickens, which allows respiratory pathogens to colonize and cause disease.

Acquiring healthy birds from the start is also a good way to prevent respiratory disease. The National Poultry Improvement Plan (NPIP) was

▾ Acquiring healthy birds from the start is a good way to prevent respiratory disease.



established in the 1930s as a cooperative state and federal program to take advantage of newfound diagnostic capabilities, identifying and reducing the incidence of *Salmonella pullorum*. This program has since expanded the scope of diseases to include *Mycoplasma (M. gallisepticum, M. synoviae, M. meleagridis)* and low pathogenic avian influenza. Many commercial hatcheries and farms conform to this voluntary program and are the ideal place to buy starter and replacement birds. Participation is often advertised, and if not, one should not hesitate to ask.

Being cognizant of biosecurity protocols can also protect a small flock from falling victim to contagious diseases. Many wild birds (e.g., sparrows, finches, etc.) that have access to the coop can spread diseases such as avian influenza, chlamydiosis, and avian tuberculosis. Exposure can also occur if chickens congregate under bird feeders when they have free-range access. Water fowl such as geese are another reservoir for avian influenza and continuously shed. Chickens are likely to seroconvert but will shed the virus for life. Despite the risk wild birds pose, acquisition

of new chickens is often the biggest risk factor for disease spread. Selecting birds from reputable suppliers that adhere to NPIP protocols is always advised. Adhering to a six-week quarantine will also allow enough time to observe if any health concerns arise before introducing birds into an existing flock.

As the seasons change, the most common respiratory diseases observed by flock owners are nonspecific respiratory infections. The typical snicks, sneezes, and coughs will be heard, but birds will often continue to eat and drink. Chickens are far less likely to look puffed up and sick as they would with other infections. Diagnostics are often not necessary as infections tend to be self-limiting and resolve within seven to 10 days. Treatment with tetracycline antibiotics may reduce duration of symptoms by half. Ensuring optimum environmental conditions is most important during this time.

A top differential for nonspecific respiratory infections is *Mycoplasma gallisepticum* (MG).

Numerous species of mycoplasma are present in the U.S. that cause disease in chickens, as well as many that act as commensal organisms. As some of these organisms can be transmitted from the hen through the egg to the chick, this is another important reason to seek out an NPIP-certified farm. Chickens affected by *Mycoplasma gallisepticum* can have mild clinical signs that typically escalate as secondary infections take hold. Snicks, sneezes, and coughing will occur in affected birds. The flock will exhibit a decreased appetite and appear fluffed and lethargic. Premortem diagnosis can be achieved by serology, PCR, or culture and identification. Necropsy will reveal air sacculitis and fibrinous polyserositis. A killed vaccine is available that will reduce clinical signs but will not prevent vertical and horizontal transmission. The standard course of treatment is injectable or water-based tylosin for a minimum of 30 days. Owners should be aware of the egg and meat withdrawal times after discontinuing antibiotic use. While clinical signs will improve, the organism is never completely cleared from the system.

Given the increased popularity of backyard chickens, it is important to inform owners about key factors that affect respiratory disease. Disease-free stock, properly ventilated housing, and appropriate biosecurity measures are not only important when raising a brood of chicks, but play an important role in maintaining a healthy flock. Owner education about common respiratory diseases is also important for early detection and treatment.

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## Update on Trimethoprim-Sulfamethoxazole, its side effects and current evidence for its use in uncomplicated urinary tract infections

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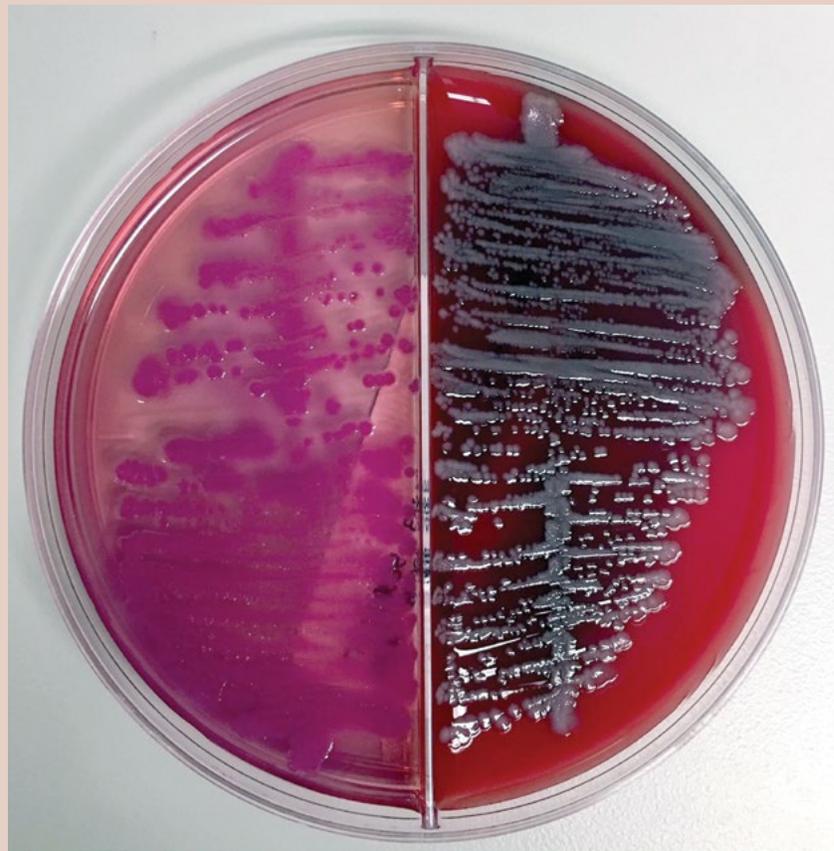
**T**rimethoprim Sulfamethoxazole (TMP-SMX) was widely prescribed in the 1970s, 1980s and 1990s. The side effect profile was limited to gastrointestinal (GI) upset or diarrhea until after market idiosyncratic drug reactions were identified. Some of the reactions reported were so unexpected and severe that many veterinarians stopped using the drug altogether in favor of drugs with more predictable side effects such as amoxicillin. This has led to wide spread use of beta-lactam antibiotics, such that in some regions of the country organisms isolated in uncomplicated urinary tract infections (UTI) are likely to be sensitive to amoxicillin only 68% of the time.<sup>1</sup> While not an unreasonable probability of success for a non-life threatening infection, the trend of increasing resistance is concerning and has inspired researchers to re-evaluate TMP-SMX as a treatment for uncomplicated UTI. While the idea of this may inspire fear in some veterinarians due to memories of reactions in bygone days, TMP-SMX may actually be singularly suited to be used for uncomplicated, often first-time UTI. This is because there is evidence that uncomplicated UTI may be cleared with short courses of antibiotics and it is likely that the most worrisome side effects may only occur with exposures to TMP-SMX longer than the recommended UTI course.

There are two types of drug reactions, dose-dependent and idiosyncratic. The dose-dependent reactions associated with TMP-SMX are thyroid suppression, hematuria and non-regenerative anemia. These reactions are thought to be due to folate depletion and are nearly always associated with either supra-therapeutic dosing (i.e. >30mg/kg/day) or prolonged courses of therapy and thus should be avoided by using TMP-SMX for only short-course therapy at recommended dosages.<sup>2</sup>

The most famous side effect of TMP-SMX use is keratoconjunctivitis sicca (KCS), and it somewhat blurs the line between dose-dependent and idiosyncratic reactions. Blepharospasm and mucoid ocular discharge are thought to occur as a result of a hypersensitivity reaction resulting

FIGURE 1

⚠ *E. coli* from a urinary specimen growing at the Angell Clinical Microbiology lab on MacConkey agar (left) and sheep's blood agar (right). Note that lactose fermentation by *E. coli* causes the MacConkey agar to turn pink.



from lymphoplasmacytic infiltration of lacrimal acinar cells which can occur during or after therapy. If KCS occurs during therapy, it may be reversible with prompt drug withdrawal since this side-effect may be in part attributable to direct cytotoxic effects to lacrimal gland tissue.<sup>2</sup> It is reasonable to check a Schirmer tear test in at-risk dogs before starting therapy, and avoid treatment in dogs with borderline values (i.e. 15mm in 60 seconds) or in dogs with excessive corneal

exposure (i.e. brachycephalic breeds) or a prior diagnosis of KCS. While KCS is not uncommon, it has not been reported in dogs on TMP-SMX for less than 5 days, again making the short courses recommended for uncomplicated UTI attractive when considering this side effect.

True idiosyncratic reactions to the sulfamethoxazole component of TMP-SMX are associated with type 2 and 3 immune-mediated reactions of various

Continued from page 10

types in dogs and humans. Dogs are theorized to be at increased risk (as compared to cats) due to reduced N-acetylation of the parent sulfonamide which may reduce clearance and lead to build-up of cytotoxic metabolites that undergo oxidation by cytochrome P450 enzymes. Specifically hydroxylamines may result in neutrophil apoptosis and be phagocytosed and presented by antigen-presenting cells along with major histocompatibility proteins, priming an immune-mediated response.<sup>2</sup> Again, these reactions are associated with at least five days of therapy. The most commonly reported reactions since use was reduced in the early 1990s (1993-2003) are fever, thrombocytopenia and hepatopathy.<sup>3</sup> It was estimated that 0.25% of dogs prescribed TMP-SMX developed reactions in one investigation, which is equivalent to 1 idiosyncratic reaction for every 400 patients treated, however again, no dog in this investigation was on TMP-SMX for less than 7 days of therapy.<sup>4</sup>

Uncomplicated urinary tract infection (UTI) is defined as, “a sporadic bacterial infection of the bladder in an otherwise healthy individual with normal urinary tract anatomy and function.”<sup>5</sup> Additionally, the animal should have clinical signs referable to UTI such as hematuria, pollakiuria or behavioral signs of dysuria. Normal urinary tract anatomy and function refers to an animal that concentrates its urine adequately, has no other systemic illness and has no obvious or extreme conformational abnormalities on physical examination. As such, a urinalysis is required to make a diagnosis of uncomplicated urinary tract infection since urine concentrating ability must be evaluated.

Uncomplicated urinary tract infections result in the majority of veterinary antimicrobial prescriptions and are a good candidate for short-course therapy. The International Society for Companion Animal Infectious Disease recently published guidelines for the treatment of UTI in dogs and cats and “acknowledged the likelihood that a shorter treatment time ( $\leq 7$  days) may be effective” despite the fact that most vets typically treat uncomplicated UTI for 7-14 days.<sup>5</sup> Recently, two investigations showed equivalent cure rates to standard course antibiotics with three days of therapy of either TMP-SMX or enrofloxacin.<sup>6,7</sup> Since enrofloxacin is a drug commonly used to treat life-threatening infections and has a side effect profile that makes it a more favorable candidate for the multiple days of therapy needed to treat serious infections, I don't recommend using it to treat uncomplicated UTI. TMP-SMX, however, has been shown to be problematic for some dogs for 5 days or longer therapy, making it less ideal for life-threatening infections and long

and short term cure rates were equivalent between TMP-SMX 15mg/kg PO twice a day for 3 days of therapy and Cephalexin 20mg/kg PO twice a day for 10 days.<sup>6</sup> It is important to note that the long-term cure rate (recurrence at one month) was high for BOTH groups (about 50%) suggesting either that neither treatment was effective for long term cure or that the UTIs being treated were not truly uncomplicated. Since long-term cure rates are rarely evaluated in UTI in dogs and cats, we don't know what “good” looks like, and most clinicians will tell you that you can't know with the first UTI whether a dog will be a “frequent flier.” The significance of the high recurrence rate shouldn't be interpreted beyond saying that a traditional UTI therapy and the short course treatment were equivalent. Of note, in a select few dogs in the TMP-SMX group of this investigation were evaluated for anti-TMP-SMX antibodies (n=8) and for drug-specific T-cell proliferation (n=9), and none of the dogs had either anti-TMP-SMX antibodies or drug-specific T-cells.<sup>6</sup> While I consider this pilot data given the low numbers, it suggests that 3 days of TMP-SMX exposure may not be enough to generate an immune response that would result in the worrisome side-effects seen with longer courses of therapy.

Finally, TMP-SMX has been shown time and time again to be one of the single most effective oral antibiotics to treat UTI. A recent investigation evaluating susceptibility of UTI to various antibiotics found isolates from uncomplicated UTI to be susceptible to TMP-SMX 90% of the time, the highest frequency of all oral antibiotics evaluated.<sup>1</sup> Investigations looking at *E. coli* specifically (the most common cause of UTI in dogs), found that isolates were sensitive to TMP-SMX 82-83% of the time.<sup>8,9</sup>

In summary, uncomplicated UTI uniquely lends itself to short courses of antibiotic therapy due to the ability to deliver antibiotics in high concentrations to the urine, the rich blood supply to the urinary bladder, the ability to obtain microbiologic samples, and the non-life threatening nature of the infection. TMP-SMX, on the other hand, is an antibiotic best used for short course therapy (3 days or less) in dogs to reduce the likelihood of antigenic exposure. Recent evidence suggests that short antibiotic courses are a reasonable approach to treat UTI, offering support to the clinician wanting to increase compliance and reduce the client headache of treating animals with oral medications without increasing the likelihood of resistance of critically important drugs commonly used to treat life-threatening infections.

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# Hypocalcemia

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Hypocalcemia is a reduction of blood calcium concentration below normal that signifies a disturbance of one or more normal homeostatic control mechanisms. Hypocalcemia may refer to a reduction of serum total calcium (tCa) or ionized calcium (iCa). iCa accounts for ~56% of tCa concentration in dogs and ~52% of tCa concentration in cats. iCa is the most important biologically active fraction of calcium. Measurement of tCa concentration is more readily available than iCa concentration (except perhaps in an emergency setting); however, correlation between these two values is often weak. In other words, tCa concentration cannot reliably predict iCa concentration. For accurate assessment of calcium status, iCa must be measured directly. Measurement of serum calcium must not be performed on blood from a lavender top or blue top tube, as EDTA and citrate will chelate the calcium and falsely decrease its value. In addition, blood sample collection and handling should be completed as anaerobically as possible, as exposure to air may increase blood pH and decrease measured iCa concentration.

Total hypocalcemia is a relatively common laboratory abnormality and is usually defined as a concentration less than 8.0 mg/dl in dogs and less than 7.0 mg/dl in cats. Measured tCa concentrations, which are affected by serum protein concentration, can be falsely increased by hemolysis and lipemia, and can be falsely decreased by hyperbilirubinemia. Ionized hypocalcemia, a reduction in the blood concentration of iCa, is generally defined as a concentration less than 1.25 mmol/L in dogs and less than 1.1 mmol/L in cats.

Clinical signs of hypocalcemia will occur only when iCa concentration is decreased. Clinical signs typically occur when iCa is less than 0.8 mmol/L. The severity of clinical signs is affected by the duration and magnitude of ionized hypocalcemia, as well as the rate of decline of iCa concentration. Since iCa stabilizes nerve cell membranes, most clinical signs of hypocalcemia are attributable to increased excitability of the central nervous system and peripheral nerves.

Hypocalcemia may range from an asymptomatic condition to one requiring emergency treatment. Clinical signs of ionized hypocalcemia in dogs and cats are usually acute and neurologic or neuromuscular in nature, including muscle tremors/fasciculations, more sustained muscle cramping, muscle rigidity, stiff gait, weakness, ataxia, facial rubbing and biting/licking paws (presumably due to paresthesia), generalized seizures, nervousness, excessive panting, irritability, and disorientation. Elevated nictitating membranes may be seen in cats. Polyuria, polydipsia, gastrointestinal signs (poor appetite, vomiting, diarrhea), and formation of lenticular cataracts are sometimes seen. Ionized hypocalcemia may also have cardiovascular effects, including hypotension, tachycardia, and left-sided myocardial failure. In severe cases, hypocalcemia can be fatal, as a result of hypotension, decreased myocardial contractility, and paralysis of respiratory muscles.

administration, alkali administration (e.g. sodium bicarbonate), and laboratory error. Hypocalcemia may also be seen in cases of sepsis, SIRS, and massive blood transfusion.

For a patient exhibiting clinical signs of hypocalcemia, emergency treatment consists of intravenous calcium supplementation. 10% calcium gluconate should be administered at a dose of 0.5-1.5 ml/kg (5-15 mg/kg) slowly to effect over 15-30 minutes, with continuous electrocardiogram (ECG) monitoring (Figure 1). The infusion should be slowed or discontinued if bradycardia, ventricular premature complexes (VPCs), and/or shortening of the Q-T interval are noted. Once clinical signs have improved, IV calcium supplementation can be continued as a continuous rate infusion (CRI) at 60-90 mg/kg/day of elemental calcium (10% calcium gluconate contains 9.3 mg/ml of elemental calcium). Calcium gluconate should never be administered via a subcutaneous route, as there is potential for severe tissue necrosis.

Oral calcium supplementation can be supplied in the form of calcium carbonate (1 g = 20 mEq calcium), at a dose of 25 mg/kg PO q8-12h. Tums can serve as a source of calcium carbonate (Figure 2). Once normocalcemia is achieved, the oral calcium can be decreased and then discontinued. Chronic treatment of hypocalcemia usually requires calcitriol, a form of Vitamin D. Unfortunately, therapy with synthetic parathyroid hormone is not currently available. A loading dose of calcitriol (0.01-0.015 mcg/kg PO q12h for 4 days) is followed by a maintenance dose (0.0025-0.0075 mcg/kg PO q12h). Maximal effect is usually seen 1-4 days after initiation of treatment. The maintenance dose should be titrated to achieve normocalcemia. Vitamin D must be continued until the underlying disorder is corrected; it is therefore given life-long in certain cases.

FIGURE 1 & 2

1. 10% Calcium Gluconate. 2. Tums can serve as a source of calcium carbonate.



Etiologies of ionized hypocalcemia include primary hypoparathyroidism (immune-mediated, congenital, idiopathic, iatrogenic), acute or chronic renal disease, urinary tract obstruction, eclampsia/lactation, acute pancreatitis, ethylene glycol toxicosis, rhabdomyolysis (including severe muscle trauma and muscle necrosis secondary to envenomation), tumor lysis syndrome, intestinal malabsorption, Vitamin D deficiency, hypomagnesemia, phosphate enema

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[angell.org/nashoba](http://angell.org/nashoba)

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

■ [angell.org/directions](http://angell.org/directions) (free parking) ■ [angell.org/hours](http://angell.org/hours) ■ [angell.org/ce](http://angell.org/ce)

## ∨ BEHAVIOR SERVICE, DOG TRAINING CLASSES AND PHYSICAL REHABILITATION SERVICE MOVE INTO NEW 8,200 SQUARE FOOT SPACE AT MSPCA-ANGELL WEST



On April 2, 2018, the MSPCA-Angell West in Waltham added 8,200 square feet of newly renovated space. The new space houses Behavior services including rewards-based dog-training classes (Obedience, Agility, Nosework, Kitten Kindergarten, etc.). Registration for classes is available at [angell.org/walthamclasses](http://angell.org/walthamclasses).

### ADDITIONAL BEHAVIOR SERVICES TO AID REHABILITATION PATIENT COMPLIANCE

Director of Behavior Services, Dr. Terri Bright, works with our vets to design special curricula such as low-impact agility and weight loss classes for dogs, and Angell behaviorist Jocelyn Strassel sees clinical cases. Specific training is also available to owners whose dogs need help pre- and post-surgery to work on rehabilitation equipment, to tolerate handling, and to tolerate required periods of inactivity.

Drs. Amy Straut and Jennifer Palmer provide Physical Rehabilitation services in the new space using a pool with massage and resistance jets as well as two AquaPaws treadmills. In addition to hydrotherapy, land-based therapy, laser therapy, acupuncture, massage, and consultation and fitting of assistive devices is available via appointments 7 days per week.

[ANGELL.ORG/REHAB](http://ANGELL.ORG/REHAB)