LIVS IN PLAIN VIEW

Long Island Veterinary Specialists

Where You Refer Your Patient First Makes All The Difference

INSIDE THIS ISSUE

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VOLUME 16 - ISSUE 3

Salivary Disease

Catherine Loughin, DVM, DACVS, DACCT

The major salivary glands are the most commonly affected glands and contribute to lubricating ingesta and facilitating formation of a food bolus for passage down the esophagus. Minor salivary glands are small and drain directly into the oral cavity to keep it moist. These are rarely affected by diseases and will not be discussed in this segment.

A salivary mucocele, or sialocele, is a collection of saliva that has leaked from a damaged salivary gland or salivary duct and has accumulated in the tissues. Resultant saliva-filled cavities are lined by inflammatory connective tissue and are not true cysts. These are often noted as a fluctuant, painless swellings of the neck or within the oral cavity. Salivary mucoceles may be classified as follows:

- **Cervical Mucocele:** This is the most common type of mucocele. It is a collection of saliva in the upper neck region, under the jaw, or between the jaws. Most of the time these are unilateral and the affected side can be determined with the patient in dorsal recumbency. We can then proceed with removal of the affected glands, usually the mandibular and sublingual.
- **Sublingual Mucocele:** (also called a ranula): Another frequent location for the formation of a mucocele is on the floor of the mouth alongside the tongue. This is frequently seen in association with a cervical mucocele. We recommend removal of the mandibular and sublingual salivary glands on the affected side in addition to marsupialization.
- **Pharyngeal Mucocele:** This type of mucocele is much less common. It is essentially a variation of the cervical mucocele but the fluid accumulation is almost entirely within the caudodorsal or lateral pharynx.
- **Zygomatic Mucocele:** This is a very rare type of mucocele where saliva originates from the small zygomatic salivary glands which are located just below the eye.

Sialoceles have reportedly been caused by trauma (nonsurgical and surgical), stones, foreign bodies and cancer however, most cases have an unknown

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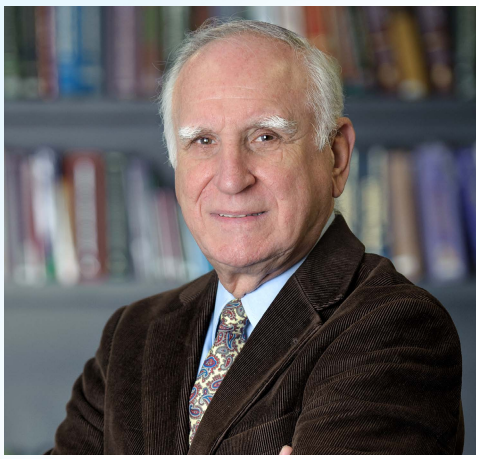
A NOTE FROM THE EDITOR



Summer 2023 is rapidly arriving and certainly welcomed by Long Islanders. LIVS has been progressing in the building modifications and the changes are smoothly blending in with the daily routines.

In March, about a dozen LIVS' members participated in a "Freezin' for a Reason" event. Team Long Island Veterinary Specialists "Took the Plunge" on March 25th at Tobay Beach for a great cause.

Owners love to reward and reinforce the bond with their pets by treats which are a way of showing love to an animal companion but..... treats can lead to a nutritional imbalance in a pet's diet if given in excess. During COVID, from 2020 to 2021, pet food became one of the best top selling consumer products goods categories in the United States; 32% of pet owners said they had purchased more pet treats during the pandemic. More than half of the respondents in the poll admitted giving their dog one to several treats a day. Another 2% admitted to giving more than 15 treats a day!

In general, high fat and high calorie treats should be avoided. Low calorie vegetable treat options that pets can eat are, sparingly, carrots, half a cucumber, green beans, celery stalks, and half a zucchini. These average 7 to 30 calories per item, but rawhide can be over 100 calories and some chew bones may be over 1000 calories! One should be careful of things like pigs' ears and pizzle sticks which can transmit salmonella and E coli, and some human foods can transmit campylobacter and toxoplasma. One must be very careful not to give xylitol, garlic, grapes, and chocolate. Xylitol can cause devastating liver injury. Scarlet chives and onions can cause gastric irritation and red blood cell damage causing anemia. Grapes and raisins cause kidney disease; chocolate can be fatal. Product quality is also very important. Items such as chicken, duck or sweet potato jerky pet treats may be imported from China and cause severe illnesses. Some foods like carrots, celery, green beans, parsnips, and summer squash contain oxalate which can cause uroliths and should not be used in those animals who have exhibited illnesses in that sphere. Fresh fruits such as blueberries and cranberries can be good low calorie treats for most dogs. They contain antioxidants, fiber, vitamin C and vitamin K, however, they are higher in sugar and calories and should be given in moderation. Giving treats is a popular way for pet owners to show affection to their pets, but it must be done in moderation.

The current increase in drug-associated events has not decreased. In 2021, approximately 70,000 deaths were attributed to fentanyl use (abuse) in humans. While intravenous fentanyl is used as an analgesic paired with a sedative for intubated patients in human and veterinary medicine, it apparently can cause something called "wooden chest syndrome" more accurately described as chest wall rigidity, (CWR). When used in anesthesia, it is a rare, idiosyncratic event. Severe hypercapnia results as the chest wall becomes rigid and its excursions are severely restricted. Fentanyl likely impacts the medullary motor center in the pons. Once the fentanyl is discontinued, thoracic excursions return to normal in about 5 minutes and recovery is generally complete.

NIH still gives grants to foreign animal testing labs that lack oversight, labs that use animals in experiments to which the National Institutes of Health has given $2.2 billion in contracts and grants from 2011 to 2021. Although the NIH requires these foreign labs to file annual reports attesting to their compliance with U.S. animal testing guidelines, it "doesn't verify the reliability of the information in these reports." While the NIH has the capacity and resources to identify and investigate risks before and while the money is awarded, it doesn't. Requiring third-party verification would cost the U.S. nothing and could make a big difference in ensuring all labs receiving funds are following the proper guidelines.

With an annual budget of $45 billion, it is unacceptable that the NIH can't be bothered with basic oversight to ensure taxpayer money isn't funding inhumane animal testing.

Meanwhile the DEA has warned that drug dealers are combining an animal sedative that can rot human tissue and lead to amputations or even death with the often-fatal synthetic opioid fentanyl. Xylazine, also known as "tranq," was

detected in 16 autopsies in Suffolk in 2022 and four in Nassau. The numbers are expected to be higher in 2023.

The Drug Enforcement Administration was asked to send a diversion control team to New York to work with local law enforcement to combat xylazine trafficking. The team would work to prevent, detect, and investigate the diversion of controlled pharmaceuticals from legitimate sources. DEA administrator Anne Milgram described xylazine as "making the deadliest drug threat our country has ever faced, fentanyl, even deadlier." Our border agents are stopping some but obviously not all illicit drug entry.

She said the federal agency "has seized xylazine and fentanyl mixtures in 48 of 50 states. The DEA Laboratory System is reporting that in 2022, approximately 23% of fentanyl powder and 7% of fentanyl pills seized by the DEA contained xylazine."

Xylazine was approved as a sedative for horses and cows in the 1970s, but it can be dangerous to humans. The DEA said people who inject drug mixtures with xylazine can develop severe wounds, including necrosis — the rotting of human tissue "that may lead to amputation."

Since xylazine is a sedative, Narcan, the lifesaving nasal spray that reverses opioid overdoses, is ineffective. But first responders and health officials should administer Narcan when someone appears to be suffering from an overdose because xylazine is frequently used to cut heroin, fentanyl and other drugs.

Law enforcement and public health officials have said that fentanyl is now responsible for the majority of fatal overdoses on Long Island as well as nationwide. Officials have warned that drug suppliers are cutting heroin with fentanyl, as well as nonopioid drugs such as cocaine. Fatal levels of fentanyl have also been found in counterfeit prescription medications, including fake Xanax and Adderall.

Something else is erupting in "the city" as the rodent population, already public enemy no. 1, poses a new threat as researchers reveal that millions of wild rats could be carrying the virus that causes COVID-19.

Being the robust rodents they are, rats given the virus inside a lab environment did not show any extreme reactions to SARS-CoV-2. Despite high levels of viral RNA within the animals' noses and lungs, none experienced weight loss or other significant reactions.

Rats likely play an important role in the evolution of Alpha, Delta, Omicron variants, which has the potential to result in the emergence of new variants in rats and may contain properties harmful to humans. The threat of future virus mutations or strains among rat populations require additional monitoring, for the protection of "both human and animal health."

With all this, we still hope the summer is joyful, healthy, and peaceful. Again, we welcome your comments e-mailed to lmarino@livs.org.

-Leonard J. Marino, MD, FAAP, LVT

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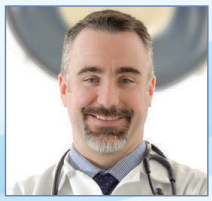

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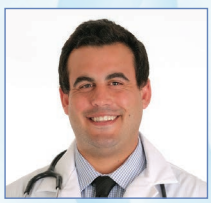

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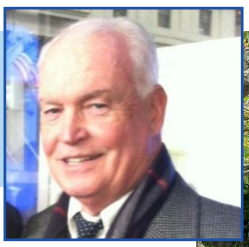

The LIVS family would like to pay tribute to our good friend and colleague, Dr. Dennis M. Farrell, who passed away on May 22, 2023. He was 71 years old.

After obtaining his undergraduate degree from the University of Pennsylvania and his veterinary degree from the University of Turin, Dr. Farrell achieved his lifelong dream of becoming a large animal veterinarian. His love and passion for horses led him to establish a private practice that stretched from Montauk to Manhattan. Dr. Farrell was an extraordinary veterinarian whose career spanned nearly four decades.

Fondly referred to as "Doc", he was a teacher and mentor to aspiring veterinarians and the entire equine community that he served. In addition to treating private clients in his practice, he was proudly the veterinarian for the NYPD mounted unit for 37 years. Throughout his life and his practice, he helped every animal and family in need. He was a brilliant veterinarian and his warmth and kindness could be felt through every animal he treated.

As Dr. Farrell always said, "It's not goodbye, it's I'll see you later."

Salivary Disease

Continued from front cover

cause. This condition is almost exclusively seen in dogs and very rarely in cats. All breeds are susceptible but there seems to be an increased incidence in Poodles, German Shepherds, Dachshunds, and Australian Silky Terriers. There is no age predisposition, and this condition may occur at any time.

Signs and Symptoms:

Generally, the development of a cervical mucocele is that of a gradually enlarging soft, painless, fluctuant mass in the upper neck or intermandibular region. In most dogs and cats there are no problems associated with the development of the mass. If the mucocele is a sublingual mucocele (ranula), the patient may have some difficulty eating and may develop bleeding from trauma to the mucocele as he or she chews. A pharyngeal mucocele is generally totally undetectable until the oral cavity is examined with sedation. Patients with pharyngeal mucoceles may experience respiratory distress because the mass developing in the throat begins to obstruct the airway (Fig 1). This is a potentially very serious problem, and treatment must be instituted rapidly because these patients may die from acute respiratory distress. Difficulty swallowing may be another sign that a pharyngeal mucocele is present. Zygomatic salivary mucocele patients present with exophthalmos, protrusion of the third eyelid, or painless orbital swelling (Fig 2).

Salivary gland neoplasia patients will present with unilateral, nonpainful, firm swelling in the region of the upper neck (mandibular gland), base of the ear (parotid gland), and upper muzzle or maxilla; halitosis, exophthalmos, and dysphagia.

Diagnostics:

Diagnosis of a sialocele or salivary gland neoplasia is usually based on clinical signs of a fluid-filled mass that contains a viscous, honey-colored, clear or blood-tinged fluid that is aspirated, or a firm non-painful mass. Other tests that can aid in the diagnosis of a sialocele or salivary gland neoplasia include radiographs, sialography, CT, MRI, ultrasonography, culture, and biopsy.

Treatment:

The treatment of a salivary mucocele is removal of the salivary gland or glands that are involved with the mucocele. Continued aspiration of a mucocele will not permanently eliminate the swelling. Recurrent aspiration also risks introducing bacteria into the mucocele, which can potentially cause an infection that will significantly increase the difficulty of successful surgical treatment.

Surgery of the mandibular and sublingual glands on the side of the mucocele is performed after confirmation of the side on imaging. The glands are removed together because the duct of the mandibular gland travels through the sublingual gland and removal of one gland would unavoidably traumatize the other. The mandibular gland is closely associated with the large veins that join to form the jugular vein. Removal of the salivary glands requires careful dissection in the area of several critically important nerves. Frequently a drain is placed in the area of the mucocele to allow fluid to escape from the area until it has a chance to heal. Sublingual mucoceles (ranulas) may be treated with marsupialization, in addition to removal of the mandibular and sublingual glands, to facilitate drainage into the oral cavity. Marsupialization is performed by excising an elliptical portion of sublingual mucosa overlying the mucocele and suturing the rim of oral mucosa to connective tissue.

Salivary gland neoplasia requires removal of the affected salivary gland and the duct. The duct is ligated during the removal process. A drain may or may not be placed depending on the location and the amount of dead space. Histopathology will determine if the mass is adenocarcinoma or acinic carcinoma, which are the most common. Other benign or malignant tumors are possible as well.

Complications:

Postoperative complications are uncommon. Occasionally a fluid pocket (seroma) may develop in the area where the mucocele was located. Infections are possible but uncommon. Recurrence is 5% or less and usually results from incomplete removal of the affected gland(s) or removal of the wrong gland. Also, sublingual swelling and bleeding may be noted. Recurrence is more likely if the gland becomes abscessed making removal of all glandular tissue more challenging.

Outcome:

Prognosis is excellent for a normal life after drainage of a mucocele and adequate removal of the affected salivary glands. Dogs do not suffer from a dry mouth following removal of the mandibular and sublingual glands, even if performed on both sides. Neoplastic prognosis is dependent on the type of tumor and how aggressive the cell types are.

Figure 1. Dog with left zygomatic salivary mucocele. He has exophthalmos and an elevated third eyelid.

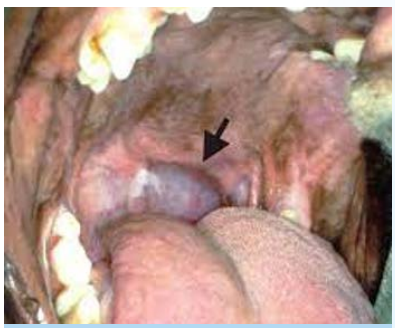

Figure 2. Dog with a left pharyngeal mucocele. This dog presented with respiratory distress, and the fluid filled pocket in the oropharynx was noted on sedated exam.

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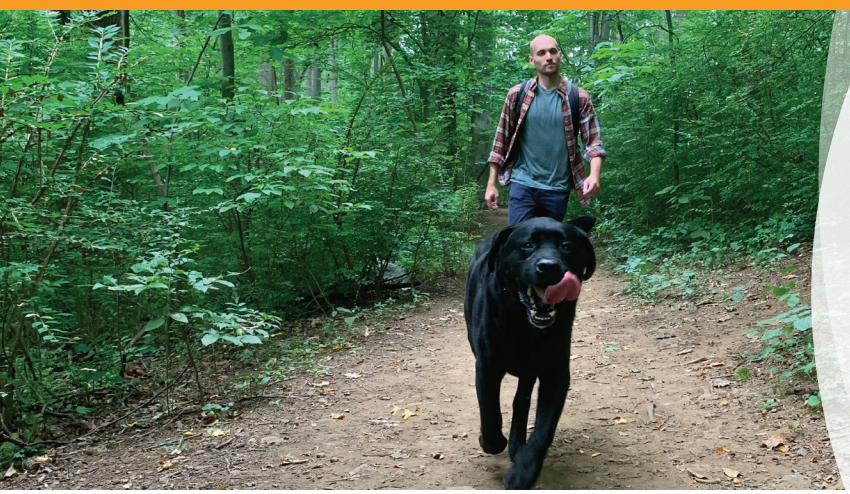
A revolution in chronic elbow OA pain management



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1. Aulakh KS, Lopez MJ, Hudson C, et al. Prospective clinical evaluation of intra-articular injection of tin-117m (117mSn) radiosynoviorthesis agent for management of naturally occurring elbow osteoarthritis in dogs: A pilot study. Veterinary Medicine: Research and Reports. 2021;12:1-12.
2. Donecker J, Fabiani M, Gaschen L, Aulakh KS. Treatment response in dogs with naturally occurring grade 3 elbow osteoarthritis following intra-articular injection of Sn (tin) colloid. PLoS ONE. 2021;16(7). e0254613.https://doi.org/10.1371/journal.pone.0254613.
3. Lattimer JC, Selting KA, Lunceford JM, et al. Intraarticular injection of a Tin-117m radiosynoviorthesis agent in normal canine elbows causes no adverse effects. Vet Radiol Ultrasound. 2019:1-8. doi: 10.1111/vru.12757.

Homogeneous Tin (^{117m}Sn) Colloid] Veterinary Device for Use in Dogs

NAME: Synovetin OA®

Tin (^{117m}Sn) stannic colloid in ammonium salt. It is supplied as a 2–4 mCi (74–148 MBq)/mL suspension for intra-articular (IA) injection.

NET QUANTITY

Vials contain a prescribed dose up to 6.0 mCi (222 MBq) at the date and time to treat one dog.1 mL of suspension contains 2–4 mCi (74–148 MBq) of tin (^{117m}Sn) stannic colloid in ammonium salt at the date and time of end use.

PRODUCT DESCRIPTION

Synovetin OA® is a conversion electron therapeutic veterinary device comprising a colloidal, sterile suspension with a pH between 6.5 and 9.0 where at least 90% of the particles have a size between 1.5 µm and 20 µm (HORIBA light scatter instrument). The ^{117m}Sn emits monoenergetic conversion electrons (significant energies 127–158 keV; emission probability 113%) and imageable gamma radiation (159 keV, 86% abundant). Accompanying low-energy emissions are Auger electrons (<22 keV) and X-rays (<30 keV). The half-life of ^{117m}Sn is 14 days. 117mSn decays by isomeric transition to stable ^{117}Sn.

Excipients include ammonium carbonate ($(NH_4)_2CO_3$), ammonium chloride (NH_4Cl), ammonium iodide (NH_4I), iodine (I_2) and trace tin (Sn) salts.

MECHANISM OF ACTION

Synovetin OA® is a veterinary device consisting of a homogeneous tin colloid which emits discrete (<300 µm) low-energy conversion electrons confined to the joint space. The colloid is composed of microparticles (1.5 µm to 20 µm) that are retained in the joint space of the dog. The particles are absorbed and retained by synoviocytes and macrophages in the synovium, resulting in apoptosis and reduction of inflammatory cells. Elimination of the pro- inflammatory cells reduces inflammation of the joint synovium, thereby reducing pain associated with synovitis. The data, including radiographic evidence, supports use in Grade 1, 2, and 3 osteoarthritis (OA) of the elbow joint.

CAUTION

Federal law restricts this device to sale by or on the order of a licensed veterinarian trained in the use of radioactive veterinary medical products. Use of this product is restricted to facilities with a compatible Radioactive Materials (RAM) license.

INTENDED USE

Synovetin OA® is intended to reduce synovitis and associated pain of canine elbow joints afflicted with osteoarthritis.

WARNINGS

Do not exceed 6.0 mCi (222 MBq) of radiation activity per dog per treatment. Not for use in humans. Keep this and all medications out of reach of children. Consult a physician in case of accidental injection or ingestion by humans.

PRECAUTIONS

Injection should be performed only by a licensed veterinarian skilled in the delivery of intra-articular (IA) injections who is located at a facility that has a RAM license.

Rigorous aseptic technique must be ensured during injection

ROUTE OF ADMINISTRATION

Intra-articular injection. The product must NOT be administered by any other route. Confirmation of needle placement is recommended, whether by anatomical landmarks, fluoroscope, C-arm, ultrasound, or radiography.

DIRECTIONS FOR ADMINISTRATION

Dogs should be appropriately anesthetized or deeply sedated prior to administration to prevent vocalization and resistance to dosing. A 22-ga. needle can be used to inject Synovetin OA® directly into the elbow joint. Pain during and after treatment may occur. Administration of non-steroidal anti-inflammatory agents at the labeled dose may help any post-treatment pain.

FREQUENCY OF ADMINISTRATION

If needed, Synovetin OA® can be readministered to a previously treated elbow at least 12 months after the last treatment.

DURATION OF EFFECT FROM ADMINISTRATION

Effectiveness has been shown to last up to 12 months following a single treatment of dogs with naturally occurring OA of the elbow.

MAXIMUM ANNUAL DOSE

Total radiation dose per joint should not exceed 3.0 mCi/joint, with the total body dose not exceeding 6.0 mCi (i.e., two elbow joints during a 12-month period).

ADVERSE REACTIONS

Dogs participating in clinical studies to evaluate safety and effectiveness (n=74 dogs, 97 elbow joints) exhibited no significant adverse reactions when administered Synovetin OA®. Discomfort in the treated elbow has been rarely reported in some dogs up to 72 hours after treatment. If adverse events are observed or suspected, please report them by calling Exubrion Therapeutics® Customer Service at 1-833-942-1247.

POST-INJECTION CARE

Following administration of Synovetin OA®, the dog can recover with other post-operation animals in the general clinic population. Once the dog has fully recovered from anesthesia, it can be discharged to go home with the approval of the facility radiation safety officer or authorized user. All treatment site policies and license requirements should be observed.

OWNER INSTRUCTIONS FOR POST-TREATMENT CARE

When the level of radiation is determined to be below the established levels for release, the dog can be discharged. The dog will, however, retain a low level of radioactivity in the treated joint(s) for a short period of time. Specific written instructions based on the post-treatment radiation dosimetry for care and proximity to the treated dog will be provided by the radiation safety officer (RSO) or authorized user (AU) of a radioactive materials (RAM)-licensed veterinary hospital to the dog owner. These instructions include information on limiting proximity to the dog in the post-treatment period. If in the judgement of the veterinarian, the dog owners are not likely to comply with the release instructions, the product should not be administered. A RAM-licensed veterinary hospital RSO or AU should contact Exubrion Therapeutics® if there are specific questions. Apart from the proximity requirements to protect people there is no requirement for restraint of the dog itself, and it can resume its normal level of activity subject to the distance requirements.

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STORAGE INSTRUCTIONS

Store in the shipping container at controlled room temperature (10°–30°C or 50°–86°F) until ready to use.

EXUBRION THERAPEUTICS

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INTEGRATIVE TREATMENT MODALITIES IN SMALL ANIMAL VETERINARY NEUROLOGY

Review of the literature and suggestions for implementation in clinical practice – Part 3

Patrick F. P. Roynard, DVM, MSc, MRCVS, DACVIM (Neurology), certified disk arthroplasty surgeon

REHABILITATION/ PHYSICAL THERAPY

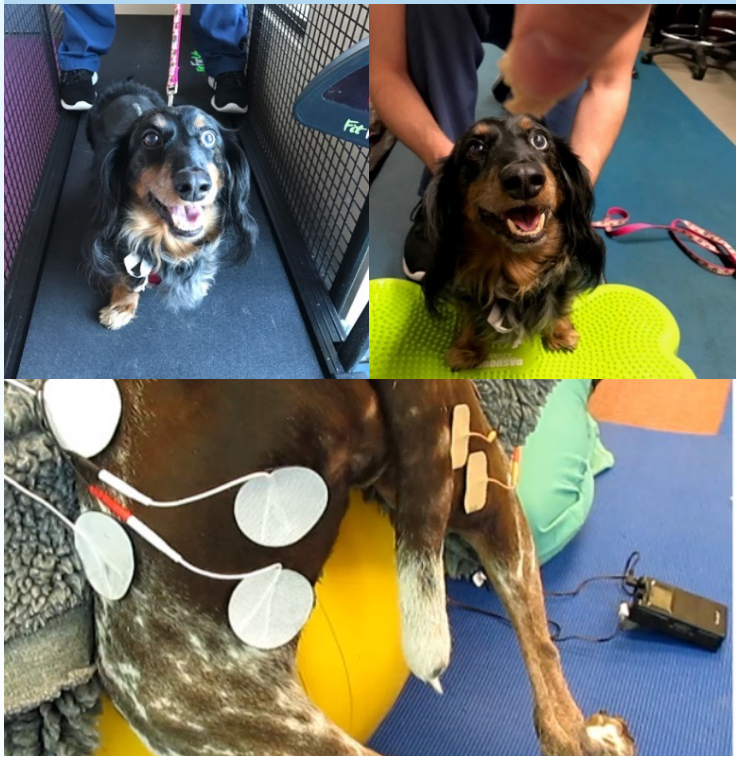
Physical activity is associated with increased levels of neurotrophins in both healthy and neurologic individuals, and exercise has been suggested to be the optimum and safest method to increase BDNF levels (Houle & Cote 2013, Weishaupt et al 2012). An increase in functional improvements has been reported with early initiation of exercise after SCI, aiming at directing neuroplasticity when the nervous system is most primed (Spejo et Oliveira 2015, Weishaupt et al 2013). The type of exercise, timing and duration of session(s) has been reported to influence effects; with early treadmill training (repetitive, sustained locomotor work) increasing BDNF that boosts functional recoveries in SCI (Hutchinson et al 2004) and stroke models (Yong et al 2017, Himi et al 2016, Ahn et al 2016). Studies have shown benefits (albeit sometimes minimal) in neuroplasticity and functional motor and sensory recovery (allodynia) when exercise is initiated early after neurologic injury (Hansen et al 2013, Hutchinson et al 2004, Fu et al 2016), with stronger improvements noted with comprehensive, multimodal rehabilitation (Yang et al 2014). This suggests that exercise such as sustained gait training modulates neuro-inflammation and stimulates neurotrophins, which is potentiated when combined with other modalities, such as neuromuscular electrical stimulation (NMES), light amplification of the stimulation of the emission of radiation (LASER) and acupuncture (Yang et al 2014, de Freitas et al 2018, Canton et al 2016, Draper et al 2012, Zheng et al 2018).

Therapeutic Exercise for SCIs

Therapeutic exercise is an essential component of any neurologic rehabilitation program. It activates and strengthens satellite cells of skeletal muscle to promote regeneration of muscle fibers following neurologic atrophy, reinforces corticospinal connections, aides in brain remodeling, and promotes neuroplasticity thereby stimulating recovery (Fu et al 2016). In animal models of SCI, treadmill training is effective at raising BDNF levels (Hutchinson et al 2004, Joseph et al 2012), which in addition to NT-3, are up-regulated in the spinal cord and skeletal muscle with treadmill exercise (Houle & Cote 2013, Gómez-Pinilla et al 2002, Gómez-Pinilla et al 2001). It is noticeable that static standing and swimming did not exhibit similar benefits (Hutchinson et al 2004). This suggests that the type and timing of exercise influences the types of neurotrophins expressed, and hence functional recovery. Studies in canine models of SCI support the positive association between BDNF and functional recovery (Han et al 2015, Lee et al 2016), with higher levels of BDNF being associated with improved recovery, which can be stimulated with sustained exercise in dogs (Brass et al 2009). However, MMP-9, a pro-inflammatory metalloproteinase, may dampen the benefits of treadmill training in promoting BDNF and NT-3 (Hansen et al 2013), highlighting the need and possible synergistic effect of using treatment modalities diminishing neuro-inflammation (such as acupuncture) concomitantly to locomotor training.

Hence, locomotor training (e.g. land treadmill) appears as an essential cornerstone for a neuro-rehabilitation program in dogs. In clinical practice, treadmill training is routinely used to initiate rhythmic locomotor movements and is relatively easy to implement (see Figure 3). In the authors' experience, patients with a remaining degree of motor function (whether ambulatory or not) benefit most from treadmill training; those with severe deficits and paralysis may show limited benefits, or even detrimental in stimulating negative neuroplasticity and/or compensation.

Figure 3. A) and B) 5YO MN Dachshund recovering from TL IVDD surgery and undergoing physical therapy with land treadmill (A) and balance exercises to help improve proprioception (B). C) Dog receiving neuromuscular electrical stimulation (NMES) on quadriceps and hamstrings while engaged in an assisted standing exercise (fNMES).



Neuromuscular Electrical Stimulation (NMES) for SCIs

NMES utilizes an electric current applied through electrodes to specific skeletal muscles or motor points, to produce contraction of the muscle (Knutson et al 2015). NMES is documented in experimental and clinical research to improve the performance of both healthy and dysfunctional skeletal muscles (Bickel et al 2011, Johnston et al 2009, Mahoney et al 2005, Stevens et al 2004, Lewek et al 2001, Ruther et al 1995). NMES is used in neurologic rehabilitation after central nervous system injury to minimize disuse atrophy, reduce muscle spasticity, facilitate the feasibility of exercise training programs, stimulate motor control improvements, and improve gait (Stein et al 2010, Harvey 2016, Bickel et al 2011).

There are differences in the recruitment and activation of motor units in skeletal muscle when comparing voluntary vs artificial-activation which are relevant when considering neurologic rehabilitation (Bickel et al 2011). NMES recruits motor units in a non-selective, spatially fixed, and temporally synchronous fashion, which leads to heightened muscle fatigue (Bickel et al 2011, Gregory & Bickel 2005). Of clinical interest, is that the non- selective recruitment noted in NMES creates the potential to activate any fiber type at low intensities, as opposed to voluntary action. The therapeutic effect of NMES, therefore, should help attenuate the muscle's response to disuse and accelerate recovery especially in the ability to target larger motor units as compared to most voluntary contractions (Bickel et al 2011). As for other modalities, its use in combination with active exercises appears to provide the most optimal functional response (Harvey 2016, Bickel et al 2011, Knutson et al 2015, Pereira et al 2012) (e.g. engaging active muscle contraction while standing/bearing weight, potentially on different surfaces, also referred to as functional neuromuscular electrical stimulation or fNMES). Such evidence again highlights the importance of using a multimodal approach including combinations of NMES, therapeutic exercises, and locomotor training for optimum recoveries (see Figure 3).

Multimodal Physical Rehabilitation programs for SCIs (e.g. canine IVDD)

Recently, several studies have been published in the veterinary literature regarding the use of physical therapy/rehabilitation in dogs recovering from TL IVDD surgery, with conflicting findings regarding results and benefits, although an overall trend towards improved recovery can be noticed. Many of these studies are retrospective, address patients that were non-ambulatory at time of presentation, involve some sort of physical therapy even in the control group (modalities such as passive range of motion or assisted standing) and they all involve multimodal therapy in the rehabilitation protocols examined (often including physical exercise such as land treadmill once the patients can stand, NMES, balance board, and occasionally laser therapy) (Zidan et al 2018, Hodgson et al 2017, Jeong &Piao et al 2019, Martins et al 2021, Bennaim et al 2017, Bruno et al 2020, Hady & Schwarz 2015).

A randomized, blinded, prospective clinical trial on 30 non-ambulatory paraparetic or paraplegic dogs (with pain perception) after decompressive surgery for TL-IVDD found that early initiation of intensive postoperative rehabilitation was safe and well tolerated. However no significant improvement in outcome was found when comparing early intensive post-operative rehabilitation (including supported standing, neuromuscular electrical stimulation (NMES), weight shifting / balance board exercises and underwater treadmill (UWT)) to less intensive post-operative treatment (ice/hot packs, passive ROM, sling walks)(Zidan et al 2018). Based on previous studies showing positive benefits of any type of locomotor training in SCIs (including ground training such as sling walks), the lack of significant differences in gait and coordination scores between the groups at days 12 and 42($P > 0.05$) may be the reflection of the fact

that both groups appear to have received some sort of locomotor training. As suggested in people with incomplete SCI, this study may reflect that overground training (i.e., sling walking) maybe equally efficacious to treadmill training in recovery of function (Zidan et al 2018). Also since standardized treatments were used, it does not appear that the intensive rehabilitation program was individually tailored to each patient. This can be problematic from a clinical perspective, because even though the dogs were of similar neurologic grades, different individuals will have variable needs and motivations, and can respond differently to various therapeutic interventions. Lastly the lack of results of this study may also reflect the importance of utilizing a diplomate from the American College of Veterinary Sports Medicine and Rehabilitation (ACVSMR) with clinical experience in neuro-rehabilitation, in order to develop appropriate and effective therapeutic interventions. The lack of significant benefits of intense neurologic rehabilitation program(s) in outcome is limited to this study, as all other published studies, albeit retrospective concluded to some benefits.

A retrospective study on 248 non-ambulatory dogs with IVDD treated via hemilaminectomy examined the influence of an in-house rehabilitation program in the post-operative management on outcome and found that a multimodal program including various combinations of underwater treadmill, land treadmill, low level laser therapy, Cavaletti drills, standing weight shifting and sit to stand exercises, pelvic limb PROM and massage, as well as cart-assisted ambulation improved the functional outcome. Rehabilitation did not accelerate recovery in this study (it is noticeable though that rehabilitation was started at a median of 14 days and a selection bias may have been introduced with more dogs with slower recovery being oriented towards rehabilitation) but was associated with a higher chance of complete recovery and a lower chance of complications. (Hodgson et al 2017). Another retrospective study comparing the outcome of dogs recovering from TL IVDD surgery based on whether they received a multimodal rehabilitation program post-operatively (RG group, n=96) or not (NRG group, n=90) found significantly ($p<0.01$) higher successful neurologic outcome in the RG group (86%, 83/96) than in the NRG group (52%, 47/90). This difference was seen for all different neurological grades considered and more pronounced in dogs with more severe deficits at presentation, with success rates in the RG group for grades 2, 3, and 4 being 97.14% (34/35), 97.33% (42/45), and 43.75% (7/16), respectively, whereas success rates were 82.35% (28/34), 51.85% (14/27), and 17.24% (5/29), respectively, in the NRG group. The RG group also recovered faster, reaching unassisted standing and unassisted walking faster than the NRG group (Jeong & Piao et al 2019). A larger retrospective controlled clinical study over 367 paraplegic dogs (with or without nociception) post-surgery for TL IVDD, divided into a study group hired prospectively and receiving intensive neurorehabilitation(n=262), and a control group obtained retrospectively and receiving "standard" physical rehabilitation, also reported a strong statistical difference in recovery of ambulation between the 2 groups($p<0.001$), along with a tendency for a difference in recovery of nociception, although this did not reach statistical significance ($p=0.058$). (Martins et al 2021). Finally, another retrospective study of 113 dogs recovering from TL IVDD surgery followed by a comprehensive rehabilitation protocol (including therapeutic exercises, [underwater] treadmill, Cavaletti rail-training, wobble-board, and NMES) found that more time in formal rehabilitation ($P < 0.001$) and more underwater treadmill sessions ($P < 0.001$) increased the chances of improvement (Hady & Schwarz 2015). However these last results must be interpreted with caution as there was no control group, the initiation of physical rehabilitation occurred with some delay following surgery, and the rates of neurologic grade improvements were lower than reported conventionally in the literature.

This trend for improvement of neurological recovery with multimodal physical rehabilitation program was also reported in cervical IVDD cases, with a retrospective study over 58 dogs recovering from ventral slot surgery for cervical IVDD reporting significantly higher successful neurologic outcome in the group undergoing rehabilitation with a combination of electrotherapy, infrared therapy, mechanical massage and treadmill exercise (27/34) compared to the group that did not receive rehabilitation (15/24)($p<0.05$) (Jeong& Rahman et al 2019).

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