LIVS IN PLAIN VIEW

Long Island Veterinary Specialists

Where You Refer Your Patient First Makes All The Difference

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VOLUME 15 - ISSUE 6

Radiosynoviorthesis using Synovetin OA® for the treatment of Degenerative Joint Disease

Dominic J. Marino, DVM, DACVS, DACCT, CCRP
ACVS Founding Fellow, Joint Replacement Surgery

Now available only at Long Island Veterinary Specialists, Synovetin OA® is a novel preparation of the radionuclide tin-117m embedded in a homogeneous colloid.

Synovetin OA® is designed for intra-articular administration to treat synovial inflammation and mitigate OA as the end stage of degenerative joint disease (DJD) in dogs. Patients are examined by an orthopedic surgeon, sedated for the administration via a simple arthrocentesis and sent home the same day with no hospitalization requirements.

Figure 1

Synovitis is the initial lesion in DJD and is instrumental in the progression to OA.

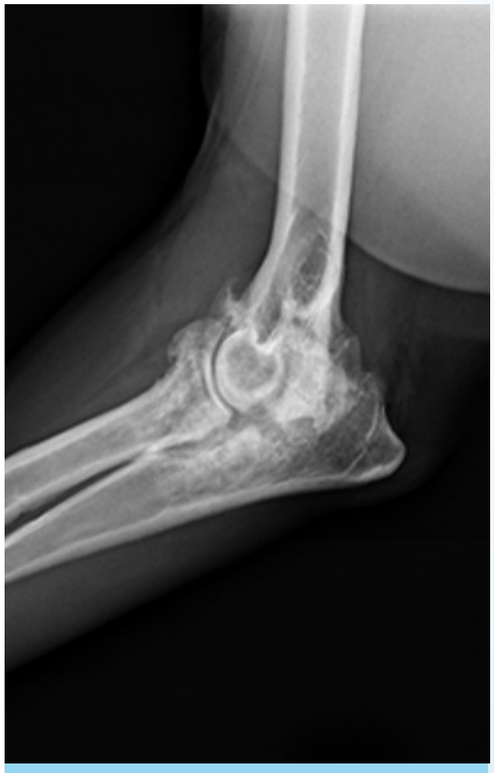

Figure 1

Synovial hyperplasia, permeability, and associated joint swelling cause acute pain and loss of joint mobility as the earliest signs of DJD.

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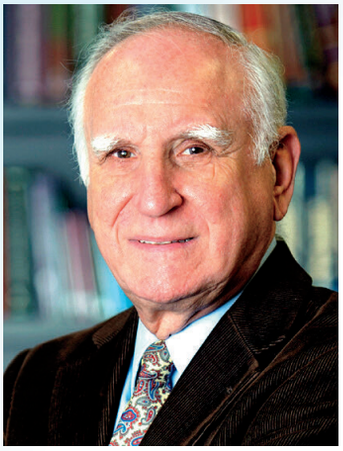
A NOTE FROM THE EDITOR

A Note from the Editor



The elections in November have again surprised many, yet as before, we will be able to move ahead on a path that leads to new ideas on how to maintain our status in the world as a leader for peace, justice, and economic stability....at least, that's the plan. The cooler weather during the last few months and the adjustments made to go out to shop rather than the delivery of "stuff" directly to our doors has led to an uptick on COVID cases on the island and together with the Flu, Monkeypox and RSV is filling hospital beds at a rate that is stretching the medical community's resources. The adjustments continue at LIVS as masks and social distancing protocols are encouraged as new virus variants emerge.

Construction is moving ahead as the building façade enlarges and remodeled areas open. The staff is expending considerable effort to keep all departments fully functioning servicing our community during the process. The K-9 memorial adjacent to the front door honors the LIVS team that was the first to appear at the 9-11 site.

As the holiday season is upon us, treats are available as usual, and vigilance must be exercised to eliminate the accessibility to items seriously dangerous to our pets. Fatty scraps, pork and poultry bones, alcoholic drinks, chocolates, sweets, and candies in general can be harmful and toxic to them. Bread dough, onions and gum containing xylitol are harmful too. Tree decorations like ornaments are tempting and could be ingested. Tinsel, lilies, mistletoe, and holly can be seriously harmful to cats especially.

Recently, a sea lion with a seizure disorder, underwent experimental brain surgery that involved transplanting healthy pig neurons into his damaged hippocampus. The patient's seizures were getting more severe and being unable to eat, his body weight dropped by nearly one-third in a few months. His health was deteriorating quickly till he had the experimental brain surgery. Since the treatment, he is seizure-free, says a neuroscientist at the University of California, San Francisco, who led the effort. Researchers say the procedure paves the way for a new strategy to treat epilepsy, but it will likely be years before the technique is attempted in people. About 1.2 percent of the U.S. population—3.4 million people—have active epilepsy. Some forms of epilepsy are debilitating, causing a person to shake uncontrollably, and become unaware of their surroundings. There are more than 30 anti-seizure medications on the market, but roughly one third of patients don't respond to them. Looks promising!

Regarding monkeypox transmission, early this summer as reported in Lancet, a 4-year-old Italian greyhound tested positive for the disease, not long after its French owners began experiencing symptoms.

They caught the virus during their non-monogamous relationship, developed ulcers, went to the Pitié-Salpêtrière Hospital in Paris for treatment after testing positive for Monkeypox while continuing to share their bed with their dog who they prevented from any contact with other pets or humans from the onset of their own symptoms. Humans to pets, though not common, can occur.

We are exceptionally grateful to both Wendy and Gail Waller who celebrated the holiday festivities at LIVS by again providing a beautiful buffet of delightfully tasty foods, salads and desserts. Their participation and assistance in the care of pets, some abandoned and all loved is boundless. We are proud to be in partnership with them in this endeavor.

We hope a peaceful holiday season will allow us to share with our loved ones the joys of life and a brighter 2023.

We are pleased to continue the extended hours for consultation in all our departments to serve our clients more efficiently. Appointments can be made through our telephone receptionists at 516 501-1700. Again, we welcome your observations e-mailed to lmarino@livs.org

-Leonard J. Marino, MD, FAAP, LVT

Where You Refer Your Patient First Makes All The Difference

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AAHA ACCREDITED REFERRAL

Radiosynoviorthesis using Synovetin OA® for the treatment of Degenerative Joint Disease

Continued from cover

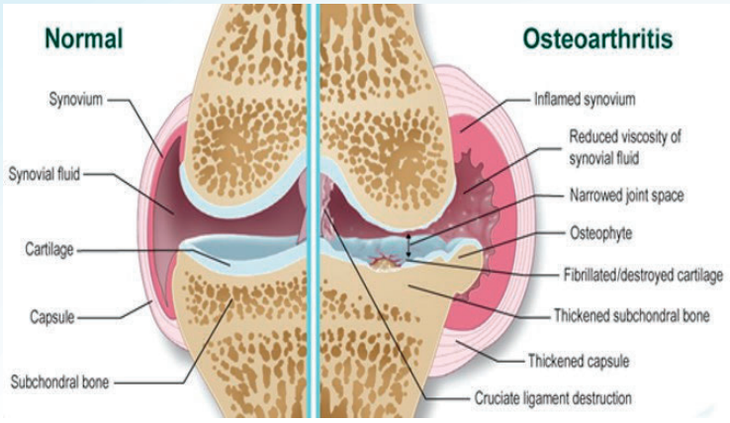


Figure 2

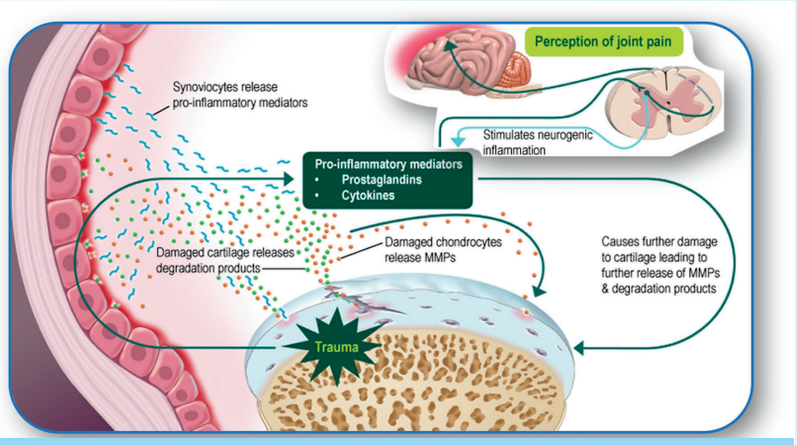


Figure 3

Figure 2

More significantly, acute or chronic synovitis can trigger a pernicious inflammatory process leading to cartilage degradation and loss. The pathophysiology of joint inflammation includes marked intra-articular overexpression of pro-inflammatory mediators and cytokines, production of chondrodestructive enzymes, synovial neovascularization, and increased C-reactive protein, a biomarker of inflammation. This inflammatory cascade activates neurons in synovial tissue as nociceptive transduction, resulting in a pain response. Given its primal role in DJD, synovitis becomes an inviting target for therapeutic intervention and a potential locus for disease modification.

Figure 3

The conventional approach to treating osteoarthritis (OA) in companion animals is anti-inflammatory or analgesic therapy following clinically acute or radiographic diagnosis. First-line OA treatment typically includes nonsteroidal anti-inflammatory drugs (NSAIDs), hyaluronic acid injection, piprants, nutraceuticals, glucocorticoids, and regenerative therapies (e.g., stem cells, platelet-rich plasma).

Synovetin OA® , a homogeneous colloid suspension of the radionuclide tin-117m, offers an alternative approach with therapeutic precision and safety. By targeting tissue critical to the genesis of the OA pathway, Synovetin OA® has significant advantages over other modalities that treat OA. As an intra-articular, single-dose, clinician-administered device, Synovetin OA® avoids systemic side effects and offers safety, convenience, and improved compliance versus agents such as NSAIDs that are given daily as chronic therapy by the pet owner.

Figure 4

Radiosynoviorthesis using Synovetin OA™ has at least two key distinctions from traditional DJD therapies such as NSAIDs, oral corticosteroids, and piprants.

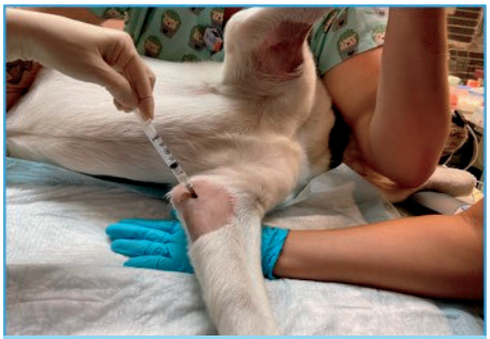


Figure 4

Although these classes of drugs provide analgesia of short duration, they are non-targeted agents in that they are distributed and metabolized systemically with the potential for unwanted side effects. Moreover, systemic anti-inflammatory agents are widely available from OTC sources and, as owneradministered treatments, have a strong potential for irregular compliance. Consistent absence of local or systemic side effects in tin-117m–treated dogs in all three trials was a strong affirmation of the safety of intra-articular injection with Synovetin OA® . Because tin-117m is phagocytized and held in situ within the synovium and has a radiologic range confined to the synovial intima thickness, its local sequestration without systemic activity is assured. This dosing precision makes Synovetin OA® a truly targeted treatment distinct from systemic OA therapies. By altering cellular composition within tissue critical to the origin of the OA pathway and the durability of a favorable treatment response, radiosynoviorthesis with Synovetin OA® potentially affects the progression of OA disease. Force plate gait analysis provided objective corroboration of significant post-treatment improvement in lameness at 1, 3, 6, and 9 months in dogs with Grade 1 and 2 OA.

Continued on Page 5

Radiosynoviorthesis using Synovetin OA® for the treatment of Degenerative Joint Disease

Continued from page 4

When used as a targeted treatment, either as a single treatment or in a multimodal protocol, Synovetin OA® can be expected to provide reduction in pain and lameness and improved QOL. This was observed in a large cohort of dogs diagnosed with elbow OA and would, presumptively, be expected in other joints as well. If you have any questions about the management of degenerative joint disease or any other surgical topic, please do not hesitate to call on us.

Figure 5

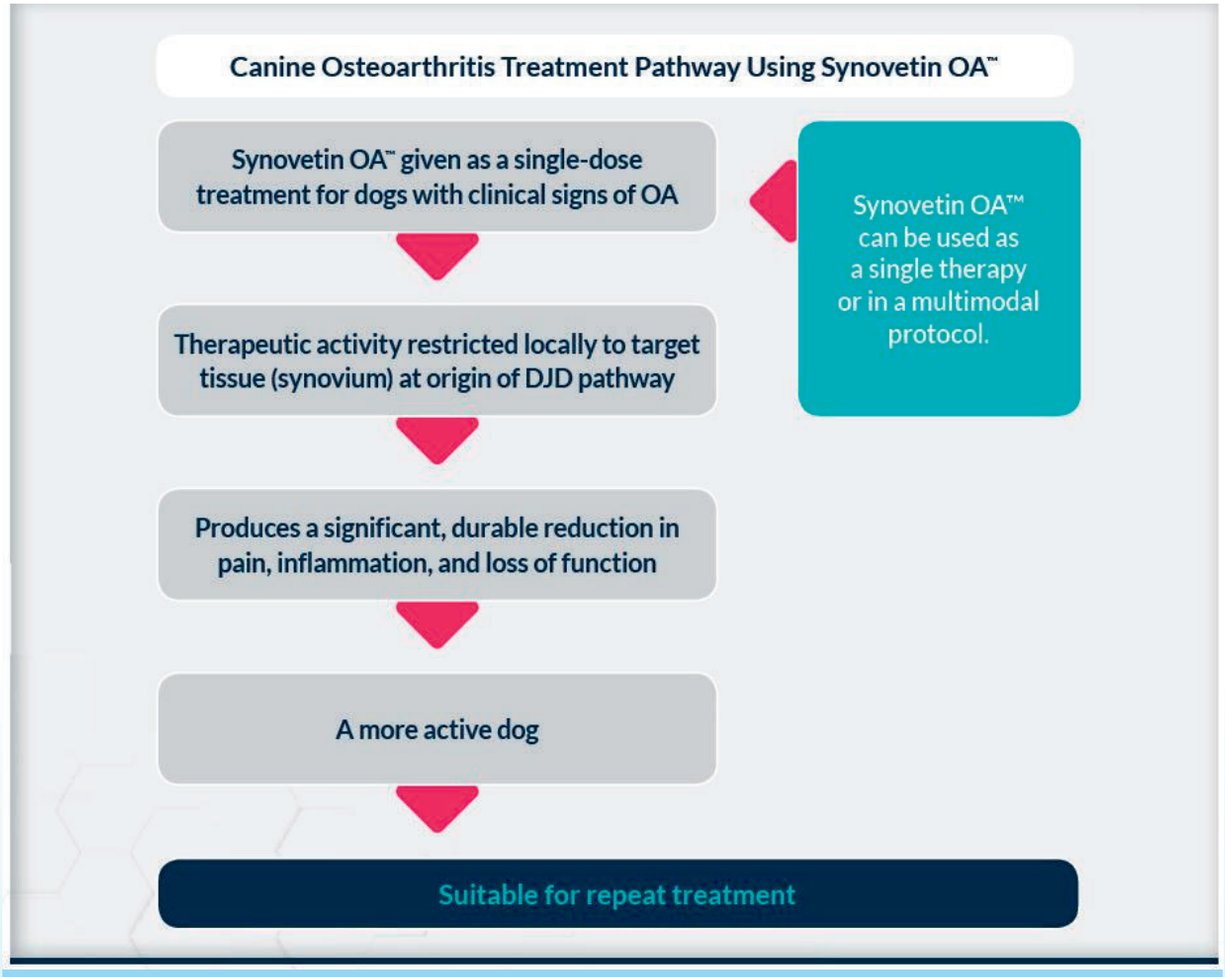


Figure 5 Canine Osteoarthritis Treatment Pathway Using Synovetin OA®

Integrative Medicine at LIVS

Veterinary Medical Manipulation (VMM)

Michel Selmer, DVM, MS, CTCVMP, CVMMP

Veterinary Medical Manipulation (VMM), is a modality that provides a very specific gentle thrust to help resolve restriction(s) and restore a normal range of motion of the joints in the body and prevent conditions from progressing.

Like Chiropractic in humans, Veterinary Medical Manipulation is a therapeutic modality that involves the manipulation and adjustment of the spine and other joints in animals to relieve restrictions. Restrictions are found by performing a motion palpation examination. Motion palpation helps to identify areas of the body that are not moving normally. If a joint becomes restricted, its ability to move in a normal range of motion is reduced and results in abnormal gait, weakened muscles, muscle spasm and tension, malnourished cartilage, and pain. Specifically, restrictions of the vertebrae can cause nerve impingement which can lead to lameness/limping, internal organ dysfunction and a depressed immune system. Veterinary Medical Manipulation is very safe and should only be performed by a trained and certified Doctor of Veterinary Medicine.

Common conditions that may respond to Veterinary Medical Manipulation:

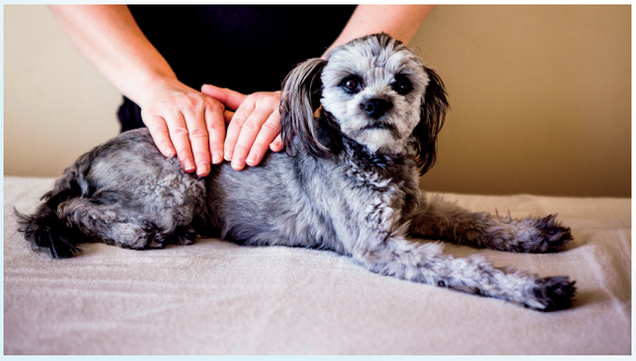
- Pain
- Weakness
- Stiffness
- Limping/Lameness
- Abnormal Posture
- Reluctance to move, jump, climb stairs, and/or exercise
- Recurrent digestive problems or incontinence
- Recurrent infections on inflammatory conditions
- Lick granulomas
- Geriatric pets to help maintain function and mobility

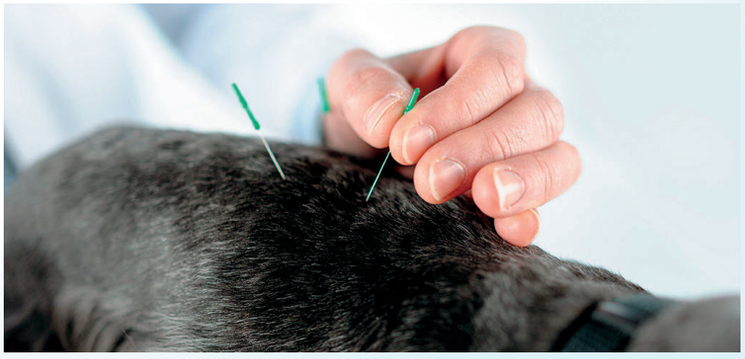
The Integrative Medicine Team takes a holistic approach to treating animal disorders. While combining techniques of both Eastern and Western medicine, our Integrative Medicine Team puts an emphasis on the patient's emotional and mental well-being. Dr. Michel Selmer is one of only a handful of Traditional Chinese Veterinary Medicine Practitioners that holds a Master's Degree in the United States.

Additional Services offered:

- Acupuncture
- Chinese Herbology
- Class IV Cold Laser Therapy
- Food Therapy
- Herbal Medicine
- Medical Manipulation (Chiropractic Care)
- Nutritional Consults
- Tui-na Massage

To refer clients to Dr. Selmer, call 516-501-1700 or visit livs.org





Management of recurrent and prolonged seizures: terminology & pathophysiology, cluster seizures (CS), status epilepticus (SE) and refractory status epilepticus (RSE) | Part 4: Refractory Status Epilepticus (RSE)

Patrick Roynard, DVM, MRCVS, DACVIM (Neurology)

Prolonged, uninterrupted seizures with resistance to conventional treatment – Refractory Status Epilepticus (SE)

Refractory status epilepticus (RSE) is defined as an onset of SE non-responsive to the standard emergency management of SE, which consists in veterinary medicine of intravenous administration of benzodiazepine (e.g. Midazolam [MZ] 0.3mg/kg IV or Diazepam [DZ] 0.5mg/kg IV) followed by another anti-epileptic medication (AEM), such as Levetiracetam (LEV) or Phenobarbital (PB). Guidelines for second medication administration include intravenous (IV) use of LEV or PB in dogs and LEV, Valproate, Lacosamide or Phenytoin in humans. Third medication studies for those cases having failed previous therapeutic steps are sparse and usually involve use of general anesthetic drugs such as Propofol. Ketamine (KET) has recently become the medication of choice at LIVS for cases of RSE (see below – treatment of RSE). Super-refractory status epilepticus (super-RSE) refers to an RSE onset that does not terminate or does recur following continuous IV administration of anesthetic agents (such as propofol) for more than 24hrs.

- Pathophysiology of RSE

GABA receptors down-regulation and benzodiazepines resistance

As for SE, RSE results from a failure of the mechanisms responsible for seizure termination under normal circumstances (see parts 1 & 3 of this newsletter), leading isolated seizure activity to progress to SE, then RSE.

The major inhibitory neurotransmitter in the brain is γ aminobutyric acid (GABA), and GABA receptors are divided into 3 categories: GABA-A, GABA-B, and GABA-Aρ (formerly known as GABA-C). GABA-A receptors are chloride-conducting membrane channels with rapid opening after stimulation by GABA. Binding of GABA to these receptors causes chloride influx and hyperpolarization of the cell, which inhibits future action potentials. Medications with GABA-A agonist effects, such as benzodiazepines and barbiturates, can terminate seizure activity and are used as first therapeutic line for this reason. During prolonged seizures in cases of SE/RSE, GABA-A receptors are both desensitized and internalized, the number of activated GABA-A receptors on the post-synaptic membrane gradually decreases while the number of inactive GABA-A receptors increases, leading to a decrease effect of GABA-ergic stimulation and ultimately resistance to benzodiazepines. The major excitatory neurotransmitter is glutamate, which binds to N-methyl-D-aspartic (NMDA) receptors. Oppositely to GABA-A receptors, the expression of NMDA receptors is up-regulated during prolonged seizures in case of SE/RSE, leading to increased number and increased activity of the NMDA receptors.

NMDA receptors are non-specific cation channels containing the NMDA and Phencyclidine (PCP) binding sites, and are also the main receptor subtype involved in glutamatergic neurotransmission.

After depolarization of the cell membrane, the combined effects of glutamate and glycine on the NMDA receptor remove the Mg^{2+} located on the inner side of the receptor, and activation of the receptor results in intracellular calcium and sodium influx through the open ion channel, responsible for the transmission and continuation of excitatory nerve impulses. Thus, prolonged seizures in cases of SE/RSE lead to a status of pharmacoresistance against the classical AEMs targeting GABAergic system for seizure termination (e.g. DZ, MZ, PB, Propofol) and potential neurotoxicity, while also triggering overexpression of NMDA receptors.

- Consequences of RSE

Consequences of RSE are similar to SE overall, with possibly magnified effects. From a central nervous system stand point and aside of the changes already described with SE (see part 3 of this newsletter) such as cerebral edema and neuronal cell death, RSE can be associated with failure of cerebrovascular autoregulation, increased intracranial pressure and decreased cerebral blood flow. From a systemic standpoint, prolonged seizure activity is accompanied by autonomic dysfunction, hyperthermia, hypoglycemia, hypoxia, hyperkalemia, hyponatremia, and hypotension. These systemic changes exacerbate neuronal injury during RSE.

- Treatment of RSE

Treatment of comorbidities: See Part 3 of this Newsletter (specific attention should be brought to regulation of temperature, cardiovascular and respiratory parameters).

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Management of recurrent and prolonged seizures: terminology & pathophysiology, cluster seizures (CS), status epilepticus (SE) and refractory status epilepticus (RSE) | Part 4: Refractory Status Epilepticus (RSE)

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Treatment of seizure: See Part 3 of this Newsletter – Figure 4 for a proposed algorithm of sequential use of injectable AEMs in cases of SE/RSE. Specifically, the normal, sequential use of AEMs applies, with first use of Diazepam (DZ), Levetiracetam (LEV) +/- Phenobarbital (PB). For cases of SE that do not terminate after several injections of benzodiazepines, RSE has developed and other therapeutic modalities should be considered.

- Propofol:
  - Very fast acting injectable anesthetic agent, it is a GABA-A agonist that acts on sites different than those targeted by benzodiazepines and barbiturates.
  - It can be used with a loading dose of 2-6mg/kg IV followed by a CRI of 0.15-0.4mg/kg/min. Cardiovascular and respiratory status of the patient should be monitored carefully and endotracheal intubation is likely to be required.
  - Propofol can be associated with seizure-like phenomena when used as anesthetic agent. One of the concerns of the author and reluctance to use propofol CRIs for SE/RSE comes from the many seizure or seizure-like events observed when lowering or discontinuing propofol CRIs. Certain studies of dogs on propofol have shown epileptic activity on EEG monitoring, raising the concern that propofol may abolish the visual effect of the seizures (convulsion) while not terminating the seizure activity at the level of the brain.
  - For these reasons, KET is the standard treatment used by the author for RSE.
- Ketamine (KET):
  - Although its complete mechanism of action is not yet fully understood, KET, a non-competitive antagonist for NMDA receptors, binds to the PCP site inside of the ion channel of the NMDA receptor. This results in blockade of the intracellular flow of Ca^{2+} and Na^{+} that normally occurs after activation of the NMDA receptor, following removal of the Mg^{2+} from the inner side of the ion channel under the combined effects of glutamate and glycine. This cellular mechanism of action is associated with reduced epileptiform burst discharges and after-potentials, resulting in inhibition of excitation conduction and anticonvulsive role, and may explain the efficacy of KET for SE/RSE in a broad range of seizure etiology.
  - In a recent study conducted at LIVS using KET 5mg/kg IV boluses for cases of SE/RSE, KET as sole agent or in combination with other AEMs such as DZ and/or LEV, resulted in termination of seizure activity in 14/14 (100%) episodes of prolonged SE (2/14) and RSE (12/14), where other AEMs or anesthetic agents classically used (e.g. DZ, PB, LEV, propofol) had previously failed.
  - This "all-or-nothing" response has been documented in other animal models of SE/RSE. The downregulation of GABA-A receptors and upregulation of NMDA receptors encountered with prolonged, uninterrupted ictal state is required for KET to be used to terminate seizure activity.
  - Although a specific time cannot be established at which this would happen for each case, the author's experience has been that this seems to occur around a half hour of uninterrupted seizure activity (potentially faster). A useful rule of thumb to remember is that "the more benzodiazepines fail, the more ketamine is likely to work".
  - Recommended dosage of KET for RSE is 5mg/kg IV bolus given once, ideally after ≥3 doses of DZ 0.5mg/kg IV (+/- other AEMs) have failed to terminate seizure event. This dosage is not anesthetic and does not trigger sedation requiring endotracheal intubation in the author's experience. Other anti-epileptic medications should be continued, as the patient may experience further seizures even after a RSE event was successfully treated with KET.

- Prognosis of RSE

Although an accurate estimation of the morbidity and mortality rate of RSE in dogs is difficult to establish, it has been associated with a mortality rate as high as 23-61% and a relapse rate of up to 90% in human survivors. This is further complicated in veterinary medicine by the frequent outcome of euthanasia solicited by care-takers in dogs surviving an onset of RSE, often for financial or perceived quality-of-life (QOL) reasons.

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Management of recurrent and prolonged seizures: terminology & pathophysiology, cluster seizures (CS), status epilepticus (SE) and refractory status epilepticus (RSE) | Part 4: Refractory Status Epilepticus (RSE)

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In the study recently completed at Long Island Veterinary Specialists on 15 dogs treated for CS, SE and/or RSE throughout 20 hospitalizations showed that 16/20 hospitalizations (80%) resulted in discharge from the hospital (with 1 case coming back within hours for persistent seizure activity) and 4/20 hospitalizations (20%) resulted in euthanasia, despite cessation of seizure activity in the hospital (all 4 patients euthanized presented at least one episode of RSE). Euthanasia was requested per owner due to a combination of prognosis associated with intracranial disease (3/4 dogs euthanized were diagnosed with structural or presumptive structural epilepsy), psychological impact of the episode of RSE on the owners, and perceived poor quality of life.

Conclusion

Occurrences of repeated (CS) or prolonged (SE, RSE) seizure activity are relatively frequent in small animal neurology. After initial treatment with benzodiazepines (e.g. Diazepam 0.5mg/kg IV, Midazolam IN or IV) and initiation of anti-epileptic medications (e.g. Levetiracetam IV bolus at 60mg/kg then relay with oral formulation at 20-30mg/kg PO TID), early referral should be considered. Despite relatively frequent relapses on the long term, prognosis can be good pending that no major systemic complication develops (e.g. aspiration pneumonia).

VETTRIAGE

After-Hours Video Telehealth Triage Services

DVM Video Sessions

24/7 video telehealth services provided by experienced, US-based veterinarians that triage client-perceived pet emergencies. Connect in minutes, no software downloads or appointments needed, connect in minutes in 3 easy steps from any computer or mobile device.

No Cost to the Clinic

VetTriage services are offered at **no cost to your clinic!** The client pays a small triage session fee to video chat with our veterinarians. Save money by eliminating the need for an after-hours answering service, whom are not medically trained and a source of frustration for the client.

Maintain Veterinary Quality of Life

Eliminate the need for a veterinarian or technician to be on-call after-hours and overnights. This has shown to **substantially improve recruitment efforts** for new vets and technicians for clinic partners.

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Nearly 80% of cases do not require a visit to the ER and the unnecessary expense associated with it. These cases are given advice and are re-directed back to the clinic for follow-up, diagnostics, and treatment. While actual emergencies are sent to the ER for immediate evaluation.

Your Cases Stay Your Cases

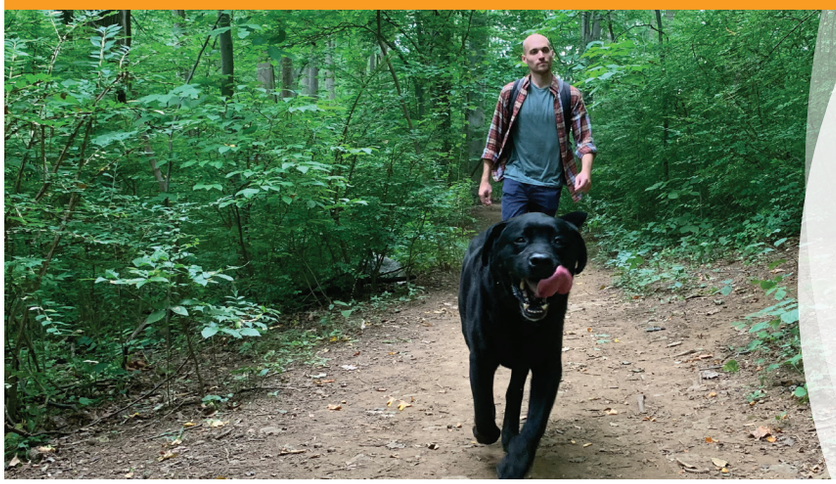
VetTriage is a **seamless extension of your clinic,** and are recommended to follow-up with you, their primary veterinarian. A session summary is emailed to both your office and your client allowing you to reference their triage session and insert it into the medical records.

Enhance Client Loyalty and Trust

Instill comfort in your current clientele that a reliable and experienced telehealth service is available during times of limited office hours and for emergency triage during after-hours, overnights, and holidays.

For more information contact our medical director Shadi Ireifej, DVM, DACVS at (845) 527-9812 or shadi.ireifej@vettriage.com

A revolution in chronic elbow OA pain management



Synovetin OA®

1 simple treatment relieves OA pain up to 1 full year.

For easy, enduring relief of chronic OA pain, use Synovetin OA.

- **Long-lasting relief:** Up to 1 full year of OA pain relief
- **Consistent effectiveness: 92%** (12/13) in mild to moderate elbow OA[1], **71%** (10/14) in severe[2]
- **Non-systemic:** No systemic adverse effects[3]
- **Convenient:** 1 simple, targeted procedure

Available here!

Long Island Veterinary Specialists

For more information, contact us at (516) 501-1700

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.

MANUFACTURED BY Theragenics Corporation for Exubrion Therapeutics®

Manufacturer's contact information:
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Customer Service Phone: 833-942-1247
info@exubrion.com

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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