LIVS IN PLAIN VIEW

Long Island Veterinary Specialists

Where You Refer Your Patient First Makes All The Difference

INSIDE THIS ISSUE

SEPT/OCT 2022
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Management of recurrent and prolonged seizures: terminology & pathophysiology, cluster seizures (CS), status epilepticus (SE) and refractory status epilepticus (RSE) - Part 3 of 4

Patrick Roynard, DVM, MRCVS, DACVIM (Neurology)

Part 3: Status Epilepticus (SE)

Prolonged, uninterrupted seizures or recurrent seizures without recovery – Status Epilepticus (SE)
Status epilepticus (SE) refers to continuous clinical or electroencephalographic seizure activity for 5 minutes or more, or to recurrent seizures/CS without recovery of normal mental status between seizures. Convulsive SE presents with impairment of consciousness and prominent motor signs, often in the form of transient or prolonged bursts of abnormal bilateral muscle contraction. Convulsive SE is the most frequent presentation of SE in both human and canine species, and can be associated with a high mortality rate in both species.

Clinically, this corresponds to patients experiencing seizures with an ictal phase (e.g. actual convulsion for generalized tonic-clonic seizures) of ≥5minutes. The other subtype of SE, non-convulsive SE, describes continuous electroencephalographic seizure activity without prominent motor symptoms and is more clearly recognized in human than veterinary patients.

-Pathophysiology of SE

Lack of termination of seizure mechanisms
SE results from a failure of the mechanisms responsible for seizure termination under normal circumstances (see part 1of this newsletter), leading isolated seizure activity to progress to SE. Neuronal excitability is affected by alterations in neurotransmitter receptor function or distribution, energy metabolism and ion flux/currents through ion channels. Persistent depolarization causes changes including altered gene expression, altered protein production, and synaptic reorganization, leading to irreversible cell damage and death. If the seizure activity continues, it may become refractory to anticonvulsant therapy (see part 4 of this newsletter).

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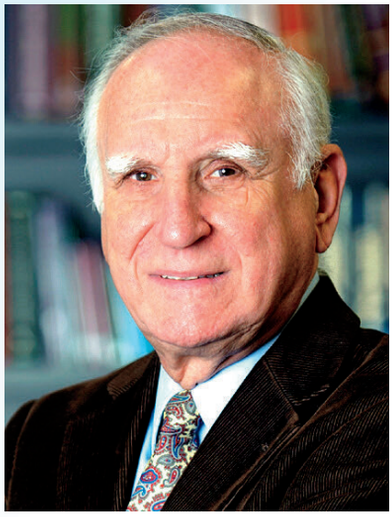
A NOTE FROM THE EDITOR

A Note from the Editor (Part 2 of 2)

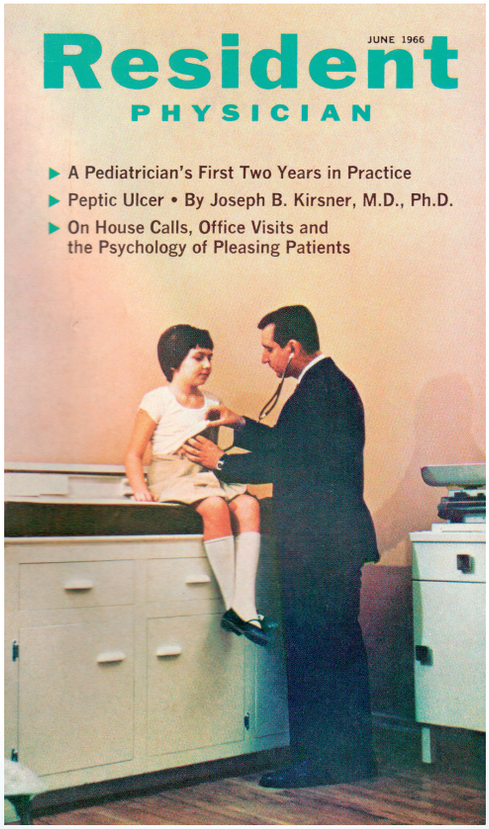


To the reader....

After graduation in 1961, internship and residency in the states followed. But in 1959, I was home for the summer for my engagement to Jane Rapisardi. She lived just a few blocks away in Queens and was just a few years ahead of my brother in St. Martin of Tours grammar school but we never met at all. 1959 was two years before graduating from medical school and I inquired at various LI Hospitals about their programs for internship. North Shore Community Hospital was then a small 250 bed local hospital and it offered only residencies, LIJ referred me to Brooklyn's Beth-El Hospital where Bela Schick was director of Pediatrics and Nassau Hospital (now NYU Langone Hospital) said I could start a rotating internship as soon as I returned. Since I was newly married in 1961 and Nassau Hospital offered living quarters and a salary of $96 a month, that was the sensible choice. Nassau Hospital had just begun accepting other than American graduates into its programs and I was made aware of how fortunate I was to be accepted -- and it was a great choice.

Disposable gloves were not in common use except in the OR and ER; IVs fluids were in glass bottles to which we added our own electrolytes; needles were resharpened, re-sterilized and re-used and syringes were glass and re-sterilized too, EKG electrodes were suction cups with a saline gel used for better contact; all was handwritten, computers were not yet invented. CT scanners, sonograms and MRIs came years later. X-Rays were taken and required developing before reading.

The hours were long; It amounted to 99 hours "on" and 69 "off". At the end of an extraordinarily busy year, Meadowbrook Hospital (now Nassau University Medical Center or NUMC) was willing to accept me into their pediatric residency program with a September starting date.



While an intern at Nassau Hospital, the $96 monthly was in need of supplementation, so on my weekends "off"', I worked from noon Saturday to Monday AM at 6 as the "house doctor" at the newly built Syosset Hospital for $2 an hour, so the additional $72 every 2 weeks helped fill the gap. That raised my hours those weeks from 99 to 135. Somehow I stayed awake and made it. Getting from Syosset to Mineola, where Nassau Hospital was located, in time for "morning rounds" or for scrubbing into the OR at 7 AM was harrowing but I was fortunate to never receive a speeding ticket.

While at Meadowbrook, I still had to moonlight at Syosset and then Hempstead General hospital, which was closer, since Meadowbrook did not provide housing. The rent was $126 a month in a one bedroom Hempstead garden apartment; our first daughter was born but at least Meadowbrook provided meals for interns, residents and family in their cafeteria on weekends! Salary was $160 a month. I informed the director at Hempstead General that we house doctors should be paid at least the same salaries as RNs.....so we got $4.00 an hour!

To be fair, gas was about 30 cents a gallon and malpractice insurance was about $200 a year; Blue Cross/Blue Shield was not much more. My new Plymouth sedan with just a radio, heater and A/T cost $2200; hospitalization, when our second child was born in 1964, was $45 a day at Nassau Hospital.

After residency, I started practice in a partnership with the then chief of Pediatrics at Central General Hospital in Plainview, Dr. Neil Palladino, a Harvard Med School graduate. He taught me what private practice was about. It had a location in both Levittown and Plainview when office visits were $5.00 with "shots" free.

A Note from the Editor (Part 2 of 2)

Continued from Page 2

All that was available was, DPT and the Salk (injectable Polio). Oral polio arrived later, was more costly and we charged $2.00 per dose when that came out. Four or five days of hospital care for a newborn was $25.00 in toto. My salary for the first year in private practice in 1964 was $12,000, and $15,000 the following year. Our first house, a new high ranch in Plainview cost $22,000. Then, the LIE only extended to Exit 58 and gas was 30 cents a gallon! Antibiotics were just Penicillin, Streptomycin and Sulfonamides. My cousin Geppy's father had died on Thanksgiving Day in 1925 of a ruptured appendix, there were no antibiotics then that could have saved him.

Pediatrics fitted me just fine. I loved it and was rewarded by being chosen by those parents who brought their children to me and by those of my peers who placed their children in my care. In 1967, after 4 children and 3 Collies, we bought a red Plymouth Fury III station wagon with many options we could not afford in 1961, cost....., $3478.80 new. It was, in my estimation, one of the most beautifully proportioned cars I ever owned. It served as the car my children brought to HS in South Huntington and I still retain a picture of it on display at home with its original hood ornament mounted on a plaque.

In 1986, my brother was stationed in Italy and he found a used, 1981 Maserati Quattroporte in great shape. With gas then at about $5.00 a gallon in Europe (it was under a dollar here in the states), anyone who could afford that could buy a new Maserati, so there was not a great big market for a used Quattroporte..... so.... for the price of a new Oldsmobile in the US, I had it shipped over and still have that exceptional car in my garage.

About 18 years ago I saw a beautiful red Alfa Romeo Spider for sale, a convertible, and for 3 years I drove that car with its 5 speed manual transmission; there is little better than being in an open car, close to the road while cruising.

My father was in his 90's then and he loved riding in the Alfa as much as in the first red soft top Plymouth.

After I became a widower, my son asked me to come work with him, specifically in the operating room at Long Island Veterinary Specialists.

I did so and enjoyed it immensely assisting mainly in total hip replacements on dogs... sometimes cats and even a pot bellied pig! In order to comply with the laws of New York State I had to be either a veterinary technician or a veterinarian to assist in the OR and so I applied for the evening and weekend program in Veterinary Science Technology at Suffolk County Community College and began the process at age 80, graduating at age 84, the oldest veterinary technician in the United States. I continue to enjoy being a surgical Licensed Veterinary Technician (MD /LVT) and it certainly keeps one's mind active.

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Management of recurrent and prolonged seizures: status epilepticus (SE)

Continued from Front Cover

- Consequences of SE

From a central nervous system stand point, SE can be associated with neuronal damages, cell apopotosis/necrosis, gliosis and network reorganization (including kindling). Prolonged seizure activity is also associated with both vasogenic and cytotoxic edema, respectively from increased blood flow (due to high metabolic demand of the seizure focus) with inflammation-triggered permeability of the blood-brain barrier and from intracellular sodium influx due to failure of the Na/K ATPase pumps.

From a systemic standpoint, prolonged seizure activity is accompanied by increased autonomic nervous system activity with increased circulating steroids and catecholamine leading to tachycardia & arrhythmias, hypertension, hyperthermia, excessive ptyalism, non-cardiogenic pulmonary edema, rhabdomyolysis (in cases of sustained excessive muscle contraction & hyperthermia) and kidney damages such as acute tubular necrosis.

-Epidemiology of SE

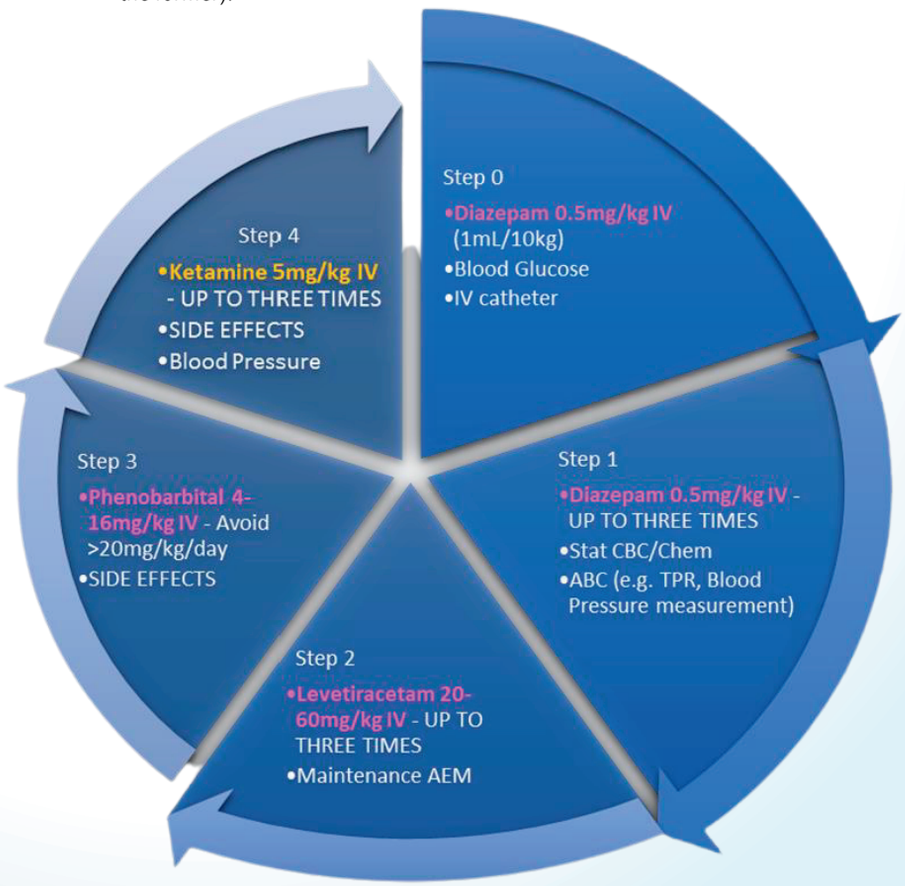
SE is a relatively common neurological emergency in both human and canine patients. In 1 veterinary study, the prevalence of dogs hospitalized for seizures and SE was 2.6% and 0.7%, respectively. SE has been reported in up to16.5% of dogs presenting for seizure activity and can be the first manifestation of a seizure disorder in 58% of dogs. It has been reported that approximately 59% of dogs with epilepsy of any kind will experience at least one episode of SE in their lifetime. Border Collies with confirmed IE are reported to have occurrences of CS in 94% and SE in 53% of the cases. Australian Shepherds with IE diagnosed before 5 years of age are reported to suffer from CS and/or SE in 80% of the cases, with almost half of the population suffering from both.

-Treatment of SE

Treatment of seizure: See Figure 4 for a proposed algorithm of sequential use of injectable AEMs in cases of SE/RSE.

- Benzodiazepines: Benzodiazepines are the first-line therapy for SE due to their fast-acting and effectiveness in terminating seizure event.
  - To terminate ictal event
    - At home, options available to the owners include the use of rectal diazepam suppository at 0.5-1 mg/kg (starting dose 0.5mg/kg if not on Phenobarbital, 1mg/kg if on Phenobarbital chronically) or intranasal Midazolam through an atomizer at 0.2mg/kg (the latter having shown better results than the former).
    - In the hospital, emergency seizure termination can be achieved with DZ 0.5-1mg/kg IV or MZ 0.2-0.5mg/kg IM/IV or intranasally if required before an IV access can be secured.
    - The author suggests using further benzodiazepine injection within minute(s) if the first one was not successful in terminating SE, and using at least 2 and up to 3 consecutive benzodiazepine injections prior to considering the need for other anticonvulsant medications to terminate SE.

Figure 4: Proposed sequential use of injectable anti-epileptic medication in cases of SE/RSE.



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Management of recurrent and prolonged seizures: status epilepticus (SE)

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        - A Diazepam or Midazolam CRI can be considered for cases when seizure activity resumes shortly after termination following benzodiazepine injection. Starting dose is 0.5mg/kg/hr for Diazepam and 0.2-0.25mg/kg/hr for Midazolam. This can be titrated up if required and should be progressively decreased after termination of the seizure event over 12-24hrs.
- Other anti-epileptic medications: In cases of SE, a daily anti-seizure medication should be started. Several options are available that can be used intravenously to "load" the patient and bypass the period of time that would normally be required for the medication to reach steady-state level in the patient's bloodstream.
    - Levetiracetam (LEV): LEV is a safe AEM for dogs and cats, both PO and/or IV. The half-life in dogs is short, approximately 2-4hrs, making this medication ideal for emergency setting. A clinical study in dogs with CS or SE showed synergistic effect of using LEV in addition to DZ compared to DZ only. The author recommends using a 60mg/kg IV LEV bolus after the first injection of benzodiazepines if it was successful to terminate the SE event or concomitantly to a second IV benzodiazepine injection if the first one was not efficient to terminate SE. A maintenance dose of 20-30mg/kg PO or IV q8hrs is recommended afterwards. This protocol, due to its practicality of use and relatively low side effects associated, is an easy way to start and maintain a patient on a first AEM in the context of SE. The initial LEV bolus can be repeated if required .
    - Phenobarbital (PB): PB can be used IV in the context of SE, to load an animal or temporarily increase the serum blood level of an animal previously on PB. PB can be administered IV as a bolus of up to 16mg/kg IV to achieve therapeutic range, however such a large dose at once is associated with severe sedation (potentially for several days). Alternatively a total of four 4mg/kg IV boluses can be administered over 24hrs (1 every 6hours), prior to a maintenance dose of 2.5-4mg/kg PO or IV q12hrs. Expected PB side effects of paresis & altered mentation (potentially lasting for few days), should be discussed with owners ahead of use.
    - Other AEMs, such as Potassium Bromide, Zonisamide, and Felbamate lack an IV formulation, rendering them unpractical in the management of SE.

Treatment of comorbidities:
During SE, several comorbidities not classically encountered in cases of isolated seizures can develop. Any patient in SE should be placed on IV fluids at maintenance rate (unless other comorbidities dictate differently).

- Hyperthermia:

For most patients with mild/moderate hyperthermia (e.g. T≤104.5F), termination of the SE event will usually recover normothermia and care should be taken not to cool the patient excessively (which could result in hypothermia). For patients with more severe hyperthermia (the authors often treats patients with T>106F on arrival), cooling measures and IV fluid therapy should be implemented at the same time as anticonvulsant therapy.

- Respiratory complications:

Dogs presenting with SE are at risk for respiratory complications (inflammation of upper airways potentially leading to obstruction [e.g. brachycephalic patients], non-cardiogenic pulmonary edema, and pneumonia). Accordingly, their respiratory rate, pattern, and temperature should be monitored during and following SE. Respiratory complications are likely to delay further diagnostic assessment of the seizure disorder, and the resulting hypoxia is likely to delay/complicate neurological recovery. They should then be treated in priority as they can decompensate quickly and engage the patient's vital prognosis. Thoracic radiographs can rule in/out pulmonary edema and pneumonia. Nasal probe for oxygen supplementation can be installed early, using the sedation provided by the use of IV Benzodiazepines. Anti-inflammatory medication (e.g. Dexamethasone SP 0.1mg/kg IV) should be considered to decrease laryngeal swelling; broad-spectrum antibiotic therapy with coupage should be started early in cases of aspiration pneumonia (chest wall/rib injuries should be ruled out first in polytrauma cases).

- Brain edema/intracranial pressure (ICP):
    - Mannitol: Mannitol is an osmotic diuretic. It acts by increasing plasma osmolality, creating an osmotic pressure gradient between intravascular space > brain extracellular space, leading to movement of free water from the brain parenchyma to the plasma, which in turn decreases ICP. As long as no contra-indication is present (e.g. severe cardiopathy, electrolytes disorder) Mannitol 1 gram/kg IV over 20-30 minutes should be administered to patients in SE, to help reduce ICP.

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Management of recurrent and prolonged seizures: status epilepticus (SE)

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- Hypertonic saline: Hypertonic saline also reduces ICP through osmotic effects. It causes intravascular volume expansion (risks are volume overload and hypernatremia). Suggested dosage is 2–4 mL/kg IV administered over 15–20 minutes.
- Dexamethasone 0.1mg/kg IV can be considered to help reduce post-ictal and vasogenic edema. This can be repeated q12-24hrs during the CS event if required.
- Furosemide: Furosemide is a loop diuretic commonly used in veterinary medicine for congestive cardiomyopathy and pulmonary edema. The author regularly uses a protocol with sequential IV injections of Mannitol 1gram/kg, Dexamethasone SP 0.1mg/kg IV or Methylprednisolone 10mg/kg IV, and Furosemide 1-2mg/kg IV (to prevent temporary overload from the combination effect of mannitol and steroids), each separated by 10-15 minutes when in need to decrease ICP.
- In cases of severe, repetitive and/or prolonged seizure activity, electrolytes abnormality and hypoglycemia can develop and should be monitored and corrected if required.

-Prognosis of SE

SE is a neurologic emergency with a high mortality rate in both humans (up to ~20%) and dogs (estimated ~25% per certain authors), with a retrospective study of 156 dogs with either SE or cluster seizures reporting that ~25% of dogs died or were euthanized during hospitalization, and up to 59% at follow-up. This justifies early and aggressive treatment, including referral if required.

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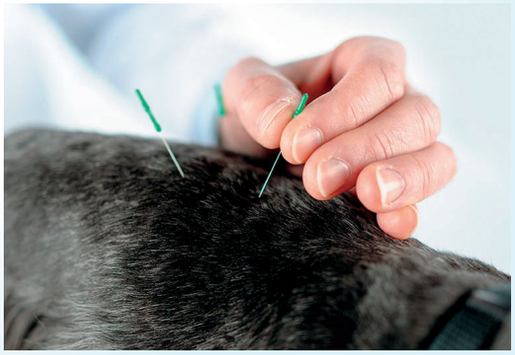
To refer clients to Dr. Selmer, call 516-501-1700 or visit livs.org



A Note from the Editor (Part 2 of 2)

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My children know that cars have always been a passion for me and for my 75th, they presented me with a 1929 Ford Model A Roadster, a car with a 4 cylinder manual shift gearbox, one that requires double clutching to change gears, and a manual spark advance, throttle control and choke setting just to get it started, yet with all that, it's a joy to drive.

Although I have in the past, installed mufflers, water pumps, radiators, tires, and other parts, I no longer do much more than wash and polish them and bring the cars to experts to tune, service, and repair. Along the way I couldn't pass on a 1947 Plymouth Special Deluxe Convertible that was for sale, one again, in that beautiful "Sumac" red color, the model and color of my first car!

To conclude this tale, I often think of how much has changed and how much has remained the same in my life, for our country and for the world. over my 90 years. My father lived before there were cars, airplanes, computers, space travel and lived through two world wars. As a car aficionado, I think of the cars that I picked up my mother in, brought my children home from the hospitals where they were born, those we rode in to go on vacations, drove to school, parties, receptions and yes, wakes and funerals. All the memories blend together and for those of us who are car enthusiasts, they are more than just transportation, each has a character and a style, and we who can hear, know they sing to us.

Leonard J. Marino, MD, FAAP, LVT

My children know that cars have always been a passion for me and for my 75th, they presented me with a 1929 Ford Model A Roadster (Figure 10), a car with a 4 cylinder manual shift gearbox, one that requires double clutching to change gears, and a manual spark advance, throttle control and choke setting just to get it started, yet with all that, it's a joy to drive.

A 1947 Plymouth Special Deluxe Convertible that was for sale, one again, in that beautiful "Sumac" red color, the model and color of my first car!

Steroid Responsive Meningitis Arteritis – Beagles, Boxers, and Beyond Part 2/2

Neil S. Mittelman, DVM, DACVIM (LAIM; Neurology)

Diagnostic Testing:

Because Steroid Responsive Meningitis Arteritis or SRMA is a systemic disorder that is not confined only to the nervous system, abnormalities are often evident on testing of blood in addition to cerebrospinal fluid. Common abnormalities on CBC include a leukocytosis characterized by neutrophilia, which was seen on 88.9% of cases in one large study. Acute phase proteins, serum proteins that increase or decrease in concentration by at least 25% in response to systemic inflammation and direct stimulation by pro-inflammatory cytokines have been studied, but their routine clinical use is hampered by a variety of reasons. C-reactive protein (CRP) has been shown to increase in both serum and CSF in dogs with SRMA; however, serum CRP is not specific and also increases in other systemic inflammatory conditions (Ex. sepsis) as well as in cases of diskospondylitis, so testing serum CRP alone is insufficient to diagnose SRMA. Albumin, a negative acute phase protein, which has been found to be significantly lower in serum of dogs with SRMA in comparison to other neurological disease also lacks specificity and likewise decrease in sepsis and other systemic infections. D- dimers are specific markers of fibrinolysis common in inflammation and vasculitis. D-dimer has been shown to be significantly increased in CSF of SRMA cases compared to other systemic inflammatory disease, but serum D-dimer elevations are significantly greater in dogs with systemic inflammatory disease than SRMA precluding serum D-dimer as a valuable serum biomarker or alternative to CSF testing in SRMA.

Antibody testing has also been shown to have some utility in testing for SRMA; however, testing blood alone is still not sufficient to make a diagnosis. Increased IgA in both serum and CSF is a valuable biomarker for SRMA in both acute and chronic stages even after treatment with corticosteroids with a sensitivity of 91% and specificity of 78% for SRMA when applying paired serum and CSF IgA results. IgA levels remain high despite clinical resolution of disease limiting its utility as a monitoring parameter. A significant difference in IgA between other inflammatory CNS disease and SRMA could also only be found in serum making it necessary to measure IgA in both serum and CSF further limiting utility.

When a young dog presents to an Emergency Service for nonspecific fever and leukocytosis, systemic evaluation often involves focal sonographic evaluation of the thorax and abdomen. It is important to recognize that significant cardiac abnormalities may be detected during this process, but the presence of abnormalities does not rule out SRMA in a dog with other supporting clinical signs. Cardiac troponin I (cTnI) is a common test of cardiac myocyte damage in dogs, but it is not specific to an underlying cause. Left ventricular systolic dysfunction, pericardial effusion and increased cTnI have all been reported in cases of SRMA. Not all dogs with SRMA have elevated cTnI (only 5/14 in 1 study) whereas spontaneous echo contrast was present in larger numbers (12/14). Spontaneous echo contrast is a characteristic swirling echogenicity of the blood in the heart chamber or blood vessels on echocardiography due to change in blood flow or hematological abnormalities (Ex. due to excessive rouleaux formation). Whereas the cardiac abnormalities listed here are not specific for SRMA nor should they be used to make a diagnosis without CBC and spinal fluid analysis, it is important to be aware that their presence does not exclude the condition from one's differential list. In fact, with appropriate corticosteroid therapy the pericardial effusion resolved in cases without need for drainage via thoracocentesis.

Imaging

Radiographic evaluation of the cervical spine would not be expected to show significant abnormalities in cases of SRMA. Given that diskospondylitis is a potential differential diagnosis radiographs are warranted especially in cases where MRI is not available. Unremarkable MRI is possible in cases of SRMA; however, common abnormalities detected include meningeal contrast enhancement alone or in addition to any of the following including cervical paraspinal musculature muscle T2 hyperintensity +/- contrast enhancement and multifocal ill-defined T2 hyperintense lesions within the cervical spinal cord with variable contrast enhancement. Meningeal enhancement is not specific for meningitis and can occur in other conditions (Ex. ischemia or neoplasia), so confirmation of diagnosis via cerebrospinal fluid analysis and testing is warranted.

Cerebrospinal Fluid Testing:

Results of cerebrospinal fluid analysis include marked neutrophilic pleocytosis with an elevated total protein in dogs with the acute form of SRMA and mild mononuclear or mixed pleocytosis with an unremarkable or slightly high total protein concentration for dogs with the chronic form.

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Steroid Responsive Meningitis Arteritis – Beagles, Boxers, and Beyond Part 2/2

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Red blood cell count may be elevated (fig. 3), and occasionally CSF may be xanthochromic due to hemorrhage (fig. 4) . Recently it has been determined that there is decreased risk of missing CSF abnormalities in SRMA when both CSF centesis is performed both at the cerebellomedullary cistern and the lumbar subarachnoid space; however, neither space alone was significantly more sensitive than the other. In older dogs this may be especially beneficial as there was a higher incidence of unremarkable CSF at one site and abnormal CSF at the other site when compared to younger counterparts.

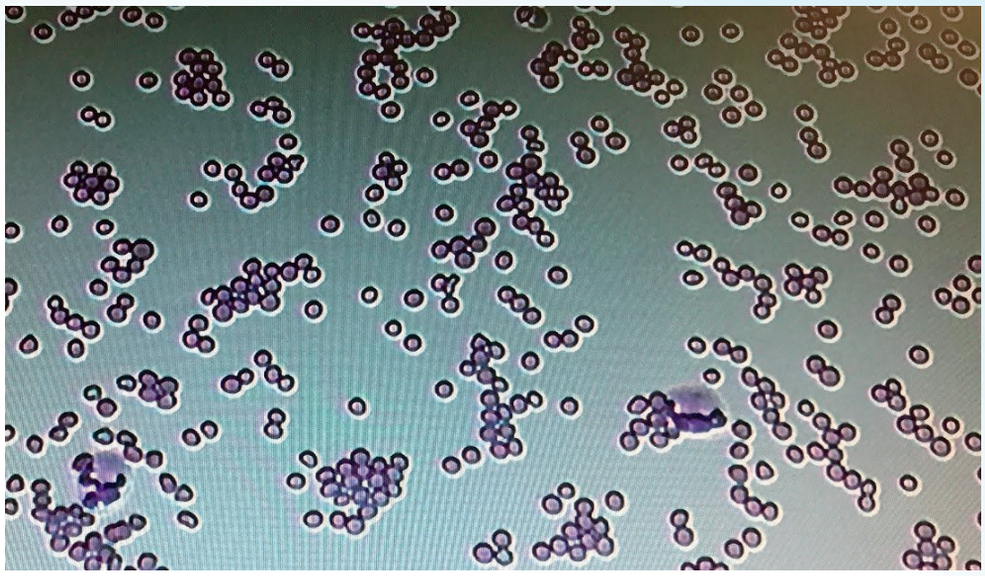

Figure 3 *Increased red blood cells in cerebrospinal fluid due to hemorrhage commonly seen in SRMA.*

Treatment

Treatment for Steroid Responsive Meningitis Arteritis includes corticosteroids. Although corticosteroid courses as short as 3 months have been advocated by some the author routinely treats for 6 months or longer. A recent retrospective study in North America revealed a median total duration of prednisone treatment of 247 days in successfully treated cases. Reported relapse rates range from 16-47.5% making it a considerable concern, and it should be noted that relapse can occur while tapering steroid dose as well as after patients have finished their prescribed course of treatment.

Some studies have failed to show significantly better outcomes in those on prednisolone monotherapy vs. prednisolone and azathioprine together; however, causative relationship and relapse cannot be determined from these studies as azathioprine is frequently added in cases of the chronic form of SRMA, which carries a higher relapse rate than the acute form. Others have showed that the concurrent use of azathioprine lowered relapse rate and allowed for accelerate steroid tapering and reduced side effects.

For those that relapse or those who fail to fully respond to corticosteroids alone additional immunosuppressant medications including but not limited to cytosine arabinoside, azathioprine, or cyclosporine are routinely used. Although no studies have showed a relationship between vaccination and SRMA or SRMA relapse the potential for triggering an excessively exuberant immune response warrants frank conversation about risks of vaccinating or not especially in a young population. These risks should be evaluated on an individual basis; however, the author does not generally advocate for vaccinating a patient that is being treated for active Steroid Responsive Meningitis Arteritis.

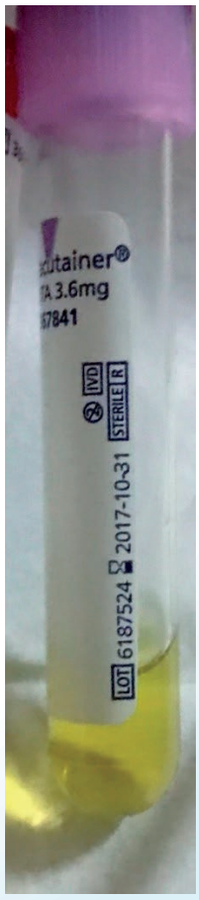

Figure 4 *Xanthochromia. Xanthochromia, a yellow discoloration of what should be normally clear cerebrospinal fluid can result from hemorrhage in cases of SRMA.*

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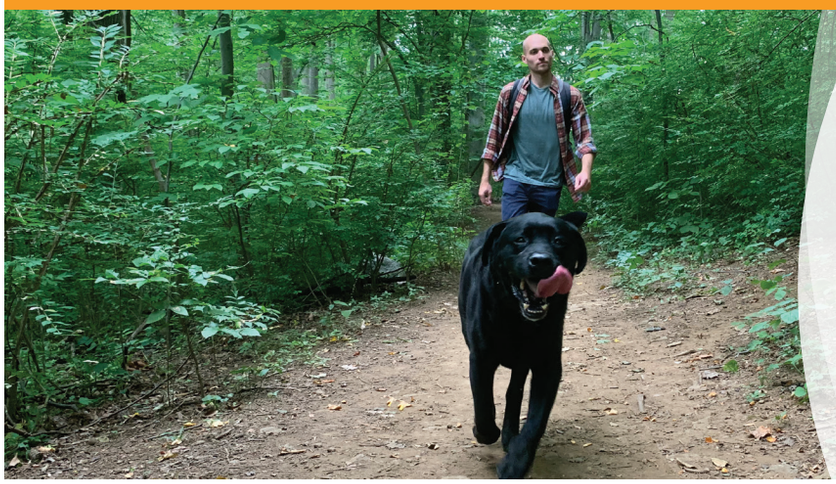
A revolution in chronic elbow OA pain management



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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.

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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:
Theragenics Corporation
5203 Bristol Industrial Way
Buford, GA 30518
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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Steroid Responsive Meningitis Arteritis – Beagles, Boxers, and Beyond Part 2/2

Continued from Page 9

Take Home Message

When evaluating a young dog with neck pain and neutrophilic leukocytosis especially if febrile Steroid Responsive Meningitis should be on the list of differentials. Other systemic signs of disease including joint inflammation and echocardiographic abnormalities occur in this systemic condition unlike other forms of autoimmune/inflammatory meningitis is dogs. A diagnosis of SRMA is based on history, CSF abnormalities, and exclusion of other diseases (Ex. diskospondylitis and sepsis). Steroid Responsive Meningitis Arteritis or SRMA has an excellent prognosis for remission and recovery if diagnosed in the acute form, but relapse is possible even after cessation of treatment.

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