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SEPTEMBER/OCTOBER 2023
VOLUME 16 - ISSUE 5

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INTEGRATIVE TREATMENT MODALITIES IN SMALL ANIMAL VETERINARY NEUROLOGY

Review of the literature and suggestions for implementation in clinical practice – Part 5

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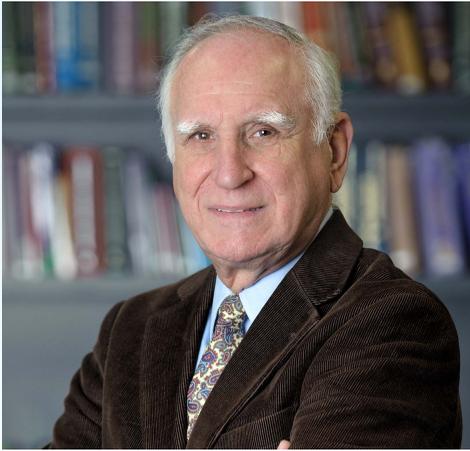
EPILEPSY/SEIZURE DISORDERS

The Yellow Emperor's Inner Classic, *Huangdi Neijing*, a two millennia old ancient Chinese medical text, considered the brain, encased in a bony skull, as a reservoir of bone marrow, the "Sea of Marrow." From a TCVM stand point, seizures are considered Internal Wind, caused

by Liver Heat (Liver Yang rising), and although certain treatment modalities can be applied to all seizure sufferers, TCVM advocates for treatment of the patient and TCVM pattern presented. Internal Wind can be related to Phlegm, Qi/ Blood Stagnation and Deficiencies of Jing, Yin and Blood. Liver Yin and Blood Deficiencies may manifest as Internal Wind and are the most common TCVM patterns in idiopathic epilepsy (Heart and Kidney are often involved as other *zang* organs) (Chrisman 2011). Idiopathic epilepsy is frequently encountered in canine neurology, and approximately 25-30% of these dogs are refractory to anti-epileptic medications (AEMs) (i.e. unsatisfactory seizure control despite two or more AEMs within therapeutic range). It is noticeable that, since these patients are not well controlled with classical treatment, they tend to be over-represented in the population of epileptics treated with alternative modalities.

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A NOTE FROM THE EDITOR



Once again, we have entered the fall season where the months are among the most colorful of the year. Although visited by a few storms, powerful hurricanes have so far skirted our island, felled fewer trees and changed our shorelines minimally. The hot summer months have passed and the sad memories of toddlers and pets who succumbed to heat stroke left in hot cars, even with windows partly open, totaled over 30 children last year; pet numbers are astounding - almost 2,000.

The events of 9/11 reminded all to honor the memory of those lost and share in the grief of their families. We also commemorated the involvement of many of the veterinarians from our area including the members of the LIVS team who responded that day by heading straight to the fallen towers and spent the first days ministering to the rescue dogs before FEMA arrived.

Fall usually seems to stimulate all that is good and bad in politics and the debates have started. This

time one of the poll leaders is not participating yet leads the pack and the incumbent is uncertain of having his party's endorsement. . . . another interesting political battle. Hopefully, our borders will become more secure as colder weather arrives and innocents are less susceptible to incidents where border patrol agents are bloodied in attacks by migrant cartel members, one of whom was an informer and even had the word "RAT" carved into his forehead. This year over 25 thousand pounds of fentanyl, 90% produced with chemicals originating from China to Mexico, came into the US, and that was just the amount caught! It only takes 2 mg. to kill an adult, less for a child, as exemplified by a recent death of an infant in a city day care facility. A priority for both parties, hopefully.

The bird flu virus — a subtype of avian influenza A called H5N1 — has sporadically infected cats in the past. It's possible that the cats had direct or indirect contact with infected birds or the birds' environments, or that they ate infected birds or food contaminated with H5N1. The risk of H5N1 exposure from cats is considered low for the general population and low to moderate for cat owners and for vets who don't use personal protective equipment.

For the first time in almost 70 years, the U.S. Centers for Disease Control and Prevention (CDC) is seeking to revise dog import regulations in an effort to keep dog rabies virus out of the U.S.

The strain most specific to dogs has not been seen anywhere in the United States since 2004 and was declared to be eliminated throughout the

nation in 2007. Being a canine rabid-free country means that dogs may still become infected from rabid wild animals like raccoons, skunks or bats, but they won't catch dog-specific rabies from another dog. The proposed changes are meant to prevent the dog-maintained rabies virus variant (DMRVV) from being reintroduced into the United States. Specifically, the CDC wants all dogs brought into the United States to have a microchip, be at least six-month of age, have proof of rabies vaccination, and have adequate serologic test results from a CDC-approved laboratory, among other requirements. "The microchip information would be included on importation documents to help ensure that dogs presented for admission are the same dogs as those listed on the rabies vaccination records." Cats are not required to have proof of rabies vaccination.

Long Island University College of Veterinary Medicine invited LIVS to host a lunch and lecture session which it did in September. Dr. Michel Selmer introduced the students to Integrative Veterinary Medicine. It was awesome with 90 plus students in attendance. LIVS sponsored not only the lecture but also provided lunch for everyone. It was a huge success and the students felt the presentation was "amazing."

We welcome your feed-back; email Imarino@livs.org

-Leonard J. Marino, MD, FAAP, LVT





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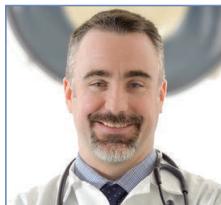
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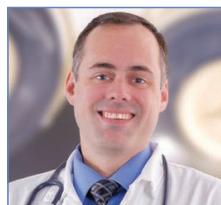
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Integrative Treatment Modalities...

Continued from front cover

Herbal medicine for seizure disorders

The management of refractory epilepsy is one of the more commonly studied neurological disorders in the herbal medicine literature. Some evidence includes the use of single-herbs: *Gastrodia elata* root, *Ginkgo biloba*, *Cannabis sativa* and formulations of *Xi Feng* (Zhu et al 2014, Sucher 2015). The most commonly used Chinese herbal medicine for treatment of seizures is *Di Tan Tang*. It is an herbal blend which, like most herbal medicine in TCVM, contains multiple herbs, fungi and other organic/ inorganic compounds, with synergistic and balancing effects. *Di Tan Tang* includes amongst others *Citrus*, *Arisaema*, *Poria*, and *Uncaria*, which have demonstrated anti-epileptic properties in animal models (Schachter et al 2008). Recommended dosage is 0.5g per 5-10kgs every 12hrs. A prospective open-label, non-comparative clinical trial in 8 dogs with refractory presumptive idiopathic epilepsy treated with *Di Tan Tang* at 0.1g/kg PO q12hrs documented an overall mean reduction in seizure frequency of 27% ($p=0.035$) with 2 of the 8 dogs qualifying as responders ($>50\%$ reduction in seizure frequency, criteria classically applied in many AEMs studies) and 2 other dogs achieving $>40\%$ reduction in seizure frequency (Dewey et al 2020).

Acupuncture for seizure disorders

Acupuncture has been advocated for seizure management with most often recommendation for several treatments weekly to biweekly, followed by a "maintenance" treatment at lesser frequency. One drawback of treating epilepsy with dry-needle acupuncture is the requirement for frequent treatment, and most research involves electro-acupuncture (EA). Although the use of EA has traditionally not been recommended in seizure disorders (due to a suspected but unverified pro-epileptic effect), recent research has shown beneficial effects of EA in several models of epilepsy, without however a consensus on acupoints and frequency to use. A murine study documented reduced epileptic seizures with both low (10Hz/1mA) and high frequency (100Hz/1mA) EA at different acupoints ($P<0.05$), but high-frequency EA elected a greater effect (Kang et al 2013). Further research has shown that low-frequency (10Hz) EA at bilateral Gallbladder 20 (GB-20) suppressed pilocarpine induced focal epilepsy by action on the μ , δ and κ opioid receptors of the central nucleus of amygdala (Yi 2015). Furthermore, EA at Stomach-36 (ST-36) +/- Stomach-37 (ST-37) reduced spontaneous seizures and can decrease epileptogenesis by elevating the expression of GAD(67) mRNA in the dentate gyrus granule cell layer (Guo et al 2008), and by reducing mossy fiber sprouting and COX-2 levels in the hippocampus (Liu et al 2014, Liao et al 2017).

Three separate publications report success using stimulation of acupuncture points in dogs by implantation of diverse materials to treat seizures. Two to 3 mm gold wire pieces implanted at multiple acupoints were associated with a 50% or more reduction in the seizure frequency of 9/15 dogs (60%) with idiopathic epilepsy (Goiz-Marquez et al 2009). In a separate case series of 5 epileptic dogs non-responsive to anticonvulsants,

small subcutaneous gold implants placed over the calvaria on the Bladder (BL), Governing Vessel (GV) and GallBladder (GB) meridians resulted in decrease in seizure frequency after treatment in 5/5 dogs (Klide 1987). Due to the risk of signal loss and susceptibility artifacts on magnetic resonance imaging (MRI) when using gold implants, Clemmons used 1mm x 0.5mm polylactic acid beads inserted at multiple acupoints using a modified 16 gauge needle in 10 dogs with refractory epilepsy. He reported significant reduction in amplitude of EEG activity, reduction of seizures by $>50\%$ in 9/10 dogs (90%) and change in seizure characteristics from cluster seizures to singular seizures (Clemmons 2015).

Nutrition and other supplements for seizure disorders

Use of a ketogenic diet has been proven efficient in reducing seizure frequency in certain forms of human juvenile epilepsy. It has also been advocated in canine epileptic patients and 2 studies have documented the use and benefits of medium chain triglycerides (MCTs) in epileptic dogs.

A 6-month prospective, randomized, double-blinded, placebo-controlled cross-over dietary trial comparing a ketogenic medium-chain triglycerides diet (MCTD) with a standardized placebo diet in 21 chronically AEMs-treated dogs with idiopathic epilepsy showed significantly lower seizure frequency (2.31/month [0-9.89/month] vs 2.67/month [0.33-22.92/month], $P = 0.020$) and seizure-day frequency (1.63/month [0-7.58/month] vs 1.69/month [0.33-13.82/month], $P = 0.022$) with the MCTD. Three dogs achieved seizure freedom and seven had $\geq 50\%$ reduction in seizure frequency (Law et al 2015). Another 6-month multicenter, prospective, randomized, double-blinded, placebo-controlled crossover trial comparing an MCT oil as diet supplement with a control oil in 28 dogs also documented significantly lower seizure frequency (median 2.51/month [0-6.67] vs 2.67/month [0-10.45]; $P = 0.02$) and seizure-day frequency (1.68/month [0-5.60] versus 1.99/month [0-7.42], $P = 0.01$) with the MCT oil diet supplement (Berk et al 2020). Cannabidiol (CBD) products have become popular and easily available. A randomized blinded controlled clinical trial used CBD infused oil at 2.5mg CBD/kg PO q12hrs for 12 weeks in dogs with IE treated with AEM(s). A significant reduction in seizure frequency (median change 33%), was reported, although the proportion of responders ($>50\%$ reduction) was similar to the placebo group (McGrath et al 2019).

NEUROPATHIES

ACUPUNCTURE

Facial nerve (CN VII) paresis/paralysis

A Cochrane review of the human literature reported that the quality of 6 randomized controlled trials (RCT) was inadequate to allow any conclusions regarding benefits of acupuncture for facial paralysis (partly due to flaws in study design and reporting). It is noticeable however that 3 of the 6 trials that were comparing acupuncture directly against drug therapy found a significantly ($p<0.05$) higher cure rate with

acupuncture treatment (Chen et al 2010). Another systematic review and meta-analysis of 14 RCTs over 1,541 human patients, despite mentioning a high risk of bias in methodological quality of the studies reviewed, reported a significantly ($p=0.005$) increased response rate associated with acupuncture for Bell's palsy (Li 2015). Both DN and EA can be used successfully as adjunct to standard treatment for various causes of CN VII paresis/paralysis and several canine case reports document resolution of facial nerve paralysis after acupuncture; one case was idiopathic (Jeong et al 2001) and one occurred following dental procedure (Abdel-Rahman et al 2008).

Vestibular disorders (CN VIII)

Acupuncture and acupressure (applying pressure to acupoints) at Pericardium-6 (PC-6) has shown beneficial in treating nausea and vomiting associated with vestibular disorders in humans, but also in significantly reducing the symptoms and discomfort associated with dizziness, vertigo and motion sickness (Hu et al 1992, Hu et al 1995, Streitberger et al 2006, Alessandrini et al 2012, He et al 2016, White 2016, Chiu et al 2015). A human clinical trial showed immediate improvement after acupuncture for vertigo and dizziness in an emergency department (Chiu et al 2015). Functional MRI (fMRI) studies have shown that the effect of acupuncture at PC-6 on vestibular disorders is via activation of the cerebellar vestibular neuromatrix (Yoo et al 2004) and selectively evoked neural responses in limbic-cerebellar brain areas (posterior insula, hypothalamus and flocculonodular lobe of the cerebellum). These effects were found to be specific to PC-6 and lasting after stimulation was discontinued (Bai et al

2010). The stimulation of other acupoints can also exert a compensatory effect on vestibular disorders, as shown in a Guinea pig model of peripheral vestibular disease where EA at ST-36 significantly ($P<0.05$) reduced nystagmus frequency and also reduced head tilt, although the last criteria did not reach statistical significance (Hu et al 1985). Multiple canine case reports document the use of TCVM (with acupuncture and herbal) for peripheral/presumptive idiopathic vestibular disease (Fowler 2011, King 2011, Yamate 2013). Both DN and EA can be used successfully as adjunct to standard treatment for dogs with vestibular disorders.

Although a modified Epley repositioning maneuver has been described to treat canine patients affected by geriatric vestibular disease, its clinical use has not been reported in details to evaluate efficacy (Kraeling 2014).

CONCLUSION

Integrative treatment modalities can be implemented easily as alternative or ideally as complement to standard treatment in small animal neurology. Laser and acupuncture may offer alluring options to decrease neuro-inflammation and promote the best environment for neuronal recovery, while their innocuity allows safe initiation early after injury and surgery. Physical rehabilitation has become the gold standard in post-neurosurgical recovery and may offer benefits in pain management and functional recovery, specifically as used concomitantly with acupuncture. Herbal medicine, nutritional therapy and other alternatives such as CBD may be of interest in management of refractory epilepsy.

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CONGRATULATIONS TO OUR VERY OWN, DR. DOMINIC MARINO!

Dominic J. Marino, DVM, Diplomate, ACVS, is the inaugural recipient of the ACVS Foundation Lynn Wheaton Philanthropy Award. The award recognizes ACVS Diplomates who demonstrate intentional and altruistic social responsibility through their work with their community, an association, or other nonprofit organizations. Recipients give their time and talent to positively impact the quality of life of people and animals and show generosity of spirit and civic responsibility.

Dr. Marino's volunteerism, accomplishments, and accolades are impressive. His affiliations include veterinary and human medical foundations and law enforcement foundations. He is a NY State emergency medical technician (EMT). In 2009, he was awarded Certificates of Meritorious Service for "risking life in service to fellow man" from the Police Surgeons Benevolent Foundation and for "placing himself in harm's way" from the Fraternal Order of Police in NY for his actions following a vehicular accident.

Dr. Marino has served as a veterinary surgeon for many of the region's law enforcement departments for decades and is responsible for developing medical protocols for multiple jurisdictions, including police and fire departments and airports. His volunteer work with the law enforcement

community includes tactical emergency care K9 training for human physicians, nurses, EMTs, and paramedics. He is a volunteer tactical K9 medical training consultant for the ATF and FBI.

Dr. Marino was one of the first veterinary responders to the World Trade Center on September 11, 2001. The lessons learned at the site motivated his desire to improve the health care and treatment of police dogs. He trains first responders on how to save the lives of their canine partners. His programs are mandatory training in many law enforcement agencies. In 2021, Dr. Marino accepted a commission as a Major in the United States Army to expand his training to military personnel.

"Bringing honor and distinction to the veterinary profession is without question the common thread of his personal life and professional career."

—Michael E. Bergman, Esquire, Suffolk County Sheriff's Foundation Board Member





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