LIVS In Plain View

LONG ISLAND VETERINARY SPECIALISTS

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Immunosuppressive Therapy - Part 2

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Cyclophosphamide

Cyclophosphamide, a cell-cycle nonspecific nitrogen mustard derivative alkylating agent, was approved by the FDA over 50 years ago, and has since become well-established in human medicine as an antineoplastic drug and immunosuppressive agent. Cyclophosphamide has persisted as a core drug used in many small-animal cancer chemotherapeutic protocols. In contrast, after many years as one of the most commonly immunosuppressive drugs utilized to treat immune-mediated diseases in cats and dogs, the use of cyclophosphamide as an immunosuppressive agent in small-animal patients has in the past two decades essentially faded away.

Cyclophosphamide is a prodrug that is metabolized by the hepatic cytochrome P450 enzyme system to eventually form active metabolites such as 4-hydroxycyclophosphamide, 4-hydroperoxycyclophosphamide, and aldophosphamide. These metabolites can enter cell cytoplasm, where they are ultimately metabolized to phosphoramide mustard and acrolein. Phosphoramide mustard is an alkylating agent that replaces a hydrogen atom with an alkyl group on the guanine base of DNA, which interferes with nuclear DNA replication and cytoplasmic RNA transcription by forming crosslinks. Cyclophosphamide has long been reported to be a potent immunosuppressive that inhibits humoral and cell-mediated immunity, including inhibition of primary and secondary immune responses, reduction of antigen trapping in lymph nodes, and inhibition of local inflammatory responses, although in a number of experimental studies in dogs, cyclophosphamide often appears to be relatively mildly immunosuppressive compared to other drugs.

Cyclophosphamide, like most alkylating agents, can cause GI side effects, myelosuppression, and hair loss. GI signs are relatively common, and include nausea, anorexia, vomiting and diarrhea. Myelosuppression appears to be dose dependent, and is associated with both the

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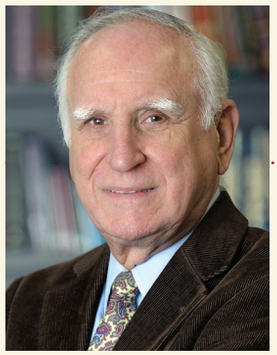
A Note from the Editor



The season that is the most colorful of the year is here and though some record acheiving days of unusual heat in early October surprised us, the somewhat cooler days, refreshing nights and back to school activities for many, fill our hours.

Plants which are being brought inside in the fall can be dangerous to our pets; especially Aloe Vera, Lily, Chrysanthemum, Philodendron spp. and others. We need to be cognizant of their harmful potential. In addition, it seems some of us, the human ones, can have a genetic variant that makes us unable to resist invasion by Capnocytophaga canimorsus. Found in pooch saliva, (and in that of felines as well) it can cause infections leading to loss of limbs and other tissues, even be fatal when one is exposed to dog saliva! Those with compromised immune systems are equally at risk.

LIVS' "class 4 Companion Laser" therapy has been functioning on a daily basis since its introduction five years ago and it continues to provides a non-invasive, pain-free treatment process that can be used to treat a variety of conditions including the reduction of inflammation, relief of arthritis pain, control of wound size and over-all healing time. It can also be performed in conjunction with existing rehabilitation and medical treatment protocols. The treatment times are very short and can easily be performed on an outpatient basis. The Therapeutic Ultrasound in our rehabilitation department has been effectively used to improve muscle elasticity, circulation and hasten bone healing; if you have any questions about the laser, U/S or the protocols, feel free to contact LIVS.

At LIVS, existing diagnostics are constantly being upgraded and we are now proud to make available a new "64 slice" CT scanner. It will be fully functional the first week of October. Its high resolution and rapid scanning times give LIVS the ability to view images with unprecedented clarity no matter the size of the pet being scanned. As always LIVS is committed to giving clients who present their pets to us, the highest standard of care.

Unchanged is the scheduled variety of total hip replacement procedures; recently in September, this editor was involved assisting in one in a nine pound "cock a poo" and another in an 88 pound Golden Mix. Both went home moving freely, thankfully, as did I.

We are all aware of the enormity of the events of 9/11 and on its 18th anniversary, we honor the memory of those lost and remember with pride the involvement of many of the veterinarians from our area especially the members of the LIVS team that answered the call that day. Our hospital administrator, Mr. Brian McKenna and the chief of staff, Dr. Dominic Marino responded at the request of the NYPD and were serving the canine contingent at "ground zero" for several days before FEMA arrived. Approximately 200 dogs were involved in the search and rescue mission, which were ably cared for by our veterinary community at the site. We thank and recognize all that was sacrificed and remember those who did not come home.

LIVS is looking forward to its upcoming Platinum Series CE on October 29th at the Crest Hollow Country Club. The topics are varied and timely. Details were mailed out and we expect a full house as before.

We are pleased to continue the extend 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.

We welcome your feed-back, e-mailed to lmarino@livs.org

Leonard J. Marino, MD, FAAP, LVT

Immunosuppressive Therapy - Part 2

➤ *Continued from Front Cover*

use of high drug doses and the use of lower doses over a sustained period of time. Myelosuppression is typically reversible with drug dose reduction or discontinuance, but can occasionally persist for weeks or even months, particularly after chronic cyclophosphamide therapy. Alopecia is most common in susceptible breeds such as poodles and old English sheepdogs. A major side effect of cyclophosphamide is sterile hemorrhagic cystitis. Cystitis is mediated by urinary excretion of acrolein. Cystitis is often debilitating to the patient, and will not resolve until the drug is discontinued. Unfortunately, cystitis can sometimes persist for days or even weeks after drug discontinuation. The chronic local bladder inflammatory effects of cyclophosphamide have also been reported to predispose to the development of irreversible bladder wall fibrosis and transitional cell carcinoma.

Over the years, a number of immune-mediated and inflammatory diseases in dogs and cats have been treated with cyclophosphamide, including immune-mediated hemolytic anemia (IMHA), immune-mediated thrombocytopenia (IMT), megakaryocyte hypoplasia, pure red cell aplasia, systemic lupus erythematosus, immune-mediated polyarthritis, inflammatory bowel disease (IBD), glomerulonephritis, noninfectious inflammatory meningoencephalitis, immune-mediated vasculitis and pemphigus. Cyclophosphamide was long considered to be a 'big gun' for dogs with severe IMHA. However, about 15 years ago, a number of case studies reported that cyclophosphamide was not better than steroids alone for the treatment of IMHA and, at worst, associated with a higher mortality rate. Given the limitations of retrospective studies, including the potential for 'case selection bias' (dogs with severe IMHA may have been given cyclophosphamide because it was perceived to be more potent), it is hard to know with any real certainty whether cyclophosphamide actually worsens prognosis in dogs with IMHA. Nevertheless, there is no doubt that, since publication of these papers, the use of cyclophosphamide to treat conditions such as canine IMHA has markedly decreased.

Cyclophosphamide is relatively cheap, with a generic 25-mg tablet costing under $2, and a 50-mg tablet costing under $4. Cyclophosphamide is difficult to dose accurately, and even more difficult to taper, especially in smaller patients. Cyclophosphamide tablets are composed of an active inner core surrounded by an inert outer shell. Because of uneven drug distribution through the tablet, cyclophosphamide tablets cannot be split without a risk of dosing inaccuracy. Without drug compounding, cyclophosphamide doses must therefore be in multiples of 25 or 50. Published immunosuppressive doses for cyclophosphamide in dogs include 50 mg/m2 or 1.5 to 2.5 mg/kg every second day or daily on a '4 days on, 3 days off' weekly protocol. In cats and small dogs, similar total weekly doses can be used, but 'pulsed' at infrequent dosing intervals that ensure that the total weekly dose is equivalent to 7x the calculated daily dose. Complete blood counts must be performed regularly throughout the course of treatment. Cyclophosphamide is available in an IV form as well as an oral form, and a recent study in dogs confirmed that equivalent oral and IV doses of cyclophosphamide achieved comparable blood levels of the active metabolite 4-hydroxycyclophosphamide. Intravenous cyclophosphamide may therefore be a viable treatment option in vomiting animals that are unable to tolerate oral immunosuppressive agents.

Chlorambucil

Chlorambucil is a nitrogen mustard derivative cell-cycle nonspecific alkylating agent that has, for many decades, been used in both human and veterinary medicine as an antineoplastic agent. Antineoplastic cytotoxicity is derived from cross-linkage of DNA and RNA by insertion of alkyl radicals on the purine base, guanine. Chlorambucil also has immunosuppressive properties, and has occasionally been used in human medicine to treat conditions such as glomerulonephritis. More than 30 years ago, some clinicians began suggesting the use of chlorambucil as an immunosuppressive agent for our small-animal patients. Since then, the use of chlorambucil for the treatment of a number of feline dermatoses, such as pemphigus and eosinophilic granuloma complex, and for IMT and refractory IBD, has become well established, perhaps because of a paucity of viable alternative medications that could be accurately dosed with safety in cats. The use of chlorambucil as immunosuppressive agent in dogs has been slower to evolve, but its use has been described for the treatment of pemphigus, glomerulonephritis and, most recently, IBD.

Chlorambucil is metabolized predominantly in the liver, primarily to the active metabolite phenylacetic acid mustard. Compared to other alkylating agents, chlorambucil is relatively well tolerated, but does occasionally cause GI side effects such as vomiting and diarrhea, and/or myelosuppression. Alopecia and poor hair growth are sometimes reported in susceptible dog breeds, such as poodles. Chlorambucil-associated neurologic signs (including myoclonus, twitches and seizures) have been reported in cats.

Chlorambucil is available as a coated 2-mg tablet that cannot feasibly be divided, and dosing recommendations in smaller patients are therefore typically provided in multiples of two, and/or 'pulsed' at infrequent dosing intervals in order to avoid overdose. Chlorambucil is almost always given in combination with a glucocorticoid. In dogs, recommended starting oral immunosuppressive chlorambucil doses range from 0.1 to 0.2 mg/kg (or, alternatively, 4–6 mg/m2) every 1–2 days. In cats (and small dogs), a starting oral chlorambucil dose of 2 mg every 2nd day, tapered to every 3rd or 4th day, is my preferred dosing immunosuppressive regime. Lower daily doses of chlorambucil, comparable to dog dosing regimens, can also be used in cats if the drug is compounded, but the effects of compounding on drug efficacy are not known. Complete blood counts must be monitored regularly and, since myelosuppression tends to be dose-dependent rather than idiosyncratic, doses can be tapered 'to effect' rather than discontinued completely.

Chlorambucil has until recently been moderately priced. Unfortunately, the patent on the only available product, Leukeran®, recently expired, leading to a change in drug company ownership, and the US price of chlorambucil has doubled as a result, to over $10 for a 2-mg tablet. There are currently no other US generic alternatives, apart from compounded products.

Azathioprine

Azathioprine has been used as an immunosuppressive agent in dogs for over 50 years. The drug was initially primarily used in studies that utilized dogs as a model for investigations of immunosuppression and organ transplantation. Within a few years, azathioprine was also being used to treat naturally occurring diseases in dogs. Despite almost half a century of clinical and research experience on the use of azathioprine in dogs, however, there have

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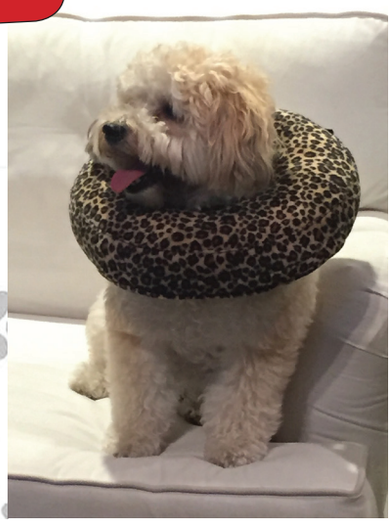

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Immunosuppressive Therapy - Part 2

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been remarkably few studies that actually elucidate the precise effects that azathioprine has on the canine immune system. Azathioprine is a prodrug for the active metabolite 6-mercaptopurine, and the primary mechanism of action was long believed to be inhibition of the synthesis of the purines adenine and guanine by blockage of enzymes such as amidophosphoribosyltranserase, with resultant production of nonfunctional nucleic acid strands. Disruption of purine synthesis inhibits DNA and RNA synthesis, thereby inhibiting the proliferation of fast-growing cells such as lymphocytes. In the past few decades, however, multiple other mechanisms of action mediated by various azathioprine metabolites have been proposed, including blockage of T-cell activation and stimulation of T-cell apoptosis. Azathioprine has long been reported to be more effective against T-cell function than B-cell function, although strong evidence supporting this is lacking.

One of the key enzymes involved in azathioprine metabolism is thiopurine methyltransferase (TPMT). Individual people inherit a marked deficiency in the TPMT enzyme that renders them highly susceptible to azathioprine toxicity. Interestingly, cats also have a marked deficiency in TPMT activity, which may explain why azathioprine causes marked myelosuppression in cats at standard canine doses. Although the use of azathioprine at a very reduced dose rates has previously been published in cats, given the narrow margin for safety it is probably wisest to recommend that azathioprine never be used in cats at any dose. Although TPMT expression in dogs is widely variable, severe deficiencies in enzyme activity of the magnitude seen in cats and some people have not been commonly reported, and TPMT deficiency does not appear to be associated with the severe drug toxicities sometimes seen in dogs.

The standard azathioprine starting dose in dogs is 2 mg/kg orally once daily. This dose is usually well tolerated and, although GI side effects such as nausea, anorexia, vomiting and diarrhea are occasionally reported, they are typically mild and self-limiting. Chronic azathioprine usage often causes a mild to moderate subclinical anemia. Uncommonly, azathioprine can also cause profound myelosuppression or severe hepatotoxicity in dogs. Myelosuppression and hepatotoxicity appear to be non-dose-dependent idiosyncratic reactions, and are typically reversible if the problem is recognized early and azathioprine is discontinued. Complete blood counts and serum biochemistry (especially ALT) should therefore be monitored regularly during azathioprine therapy. Individual case reports have reported pancreatitis in dogs receiving azathioprine, but cause and effect has not been established.

Azathioprine has become well established as an 'add-on' agent for the treatment of many different immune-mediated and inflammatory conditions when steroids alone are ineffective or poorly tolerated, including IMHA, IMT, IBD, chronic hepatitis, glomerulonephritis, immune-mediated polyarthritis, myasthenia gravis, noninfectious meningoencephalitis, immune-mediated skin diseases, and anal furunculosis. Despite decades of azathioprine usage, evidence supporting efficacy for many of these diseases is remarkably limited. One perceived 'limitation' of azathioprine compared to other immunosuppressive agents, that it can take many weeks or even months to exert its effects, is based on limited and dated data derived predominantly in humans. In my experience, azathioprine in a clinical setting exerts its immunosuppressive effects in dogs about as rapidly as most other comparable agents.

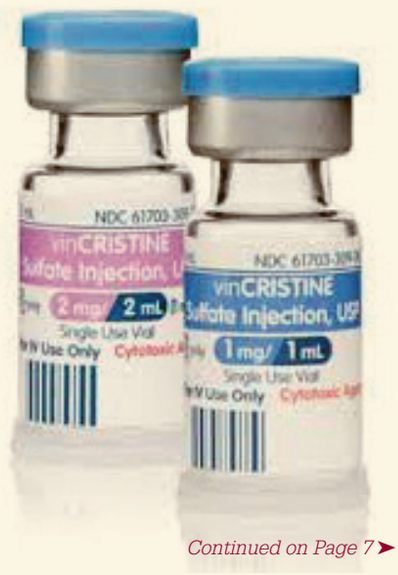
Compared to most other immunosuppressive agents, azathioprine is relatively inexpensive, which is an important consideration with long-term immunosuppressive therapy, especially in large dogs. While the proprietary product (Imuran® or Azasan®) typically still costs over $5 per 50-mg tablet, the generic equivalent can be obtained for less than $1 a tablet. The smallest tablet size is 50 mg (although tablet scoring permits a 25-mg dose), which can present dosing problems in small (under 20 lb) dogs.

Vincristine

The vinca alkaloids are biologically active, dimeric alkaloids derived from the Madagascar periwinkle plant, Catharanthus roseus. Vincristine, a naturally occurring vinca alkaloid, was characterized phytochemically more than 50 years ago. The biological effects of vincristine have traditionally been attributed to drug-induced disruption of intracellular microtubules. Microtubules are composed predominantly of complex helical polymers of the structural protein tubulin. Vincristine binds directly to tubulin, causing both inhibition of microtubule synthesis and disruption of intact microtubules. Microtubular structures susceptible to the effects of vinca-tubulin binding include the mitotic spindle in dividing cells, the neurotubules in neurons, and the cytoskeletal microtubules in platelets. Vincristine may also exert biological effects that are independent of disruption of intracellular microtubules, such as inhibition of RNA, DNA and protein synthesis, and modification of prostaglandin production.

Vincristine is a cell-cycle-specific cytotoxic agent. Vincristine disrupts microtubules within the mitotic spindle of dividing cells, thereby arresting chromosomal separation in metaphase. Vincristine at standard doses is minimally myelotoxic, and is therefore used in veterinary cancer chemotherapy in combination with more myelosuppressive agents. The degree of immunosuppression induced by vincristine at therapeutic doses is minimal compared to other immunosuppressive agents, and vincristine is therefore not used for the treatment of most immune-mediated diseases. The one exception is IMT, where vincristine has become a mainstay of treatment.

Vincristine is usually administered IV, and inadvertent SC or IM administration causes severe local tissue irritation and necrosis. Platelets, because of their intracellular tubulin, demonstrate a remarkable ability to concentrate vincristine from plasma, and are therefore the principal circulating cellular carriers of the drug. During early clinical trials in human cancer patients, it was observed that vincristine typically caused significant but transient increases



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Immunosuppressive Therapy - Part 2

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in circulating platelet numbers. A similar phenomenon has since been reported in dogs, both in research animals and in cancer patients, and appears to be due to increased megakaryocytopoiesis and thrombopoiesis, although the precise mechanisms of thrombocytosis are still uncertain. Vincristine, typically in combination with prednisone, has been reported to similarly facilitate remission of thrombocytopenia in many canine patients with IMT. Original case reports demonstrating a rapid response to vincristine in dogs with IMT have been supported, decades later, by evidence obtained from prospective studies. Circulating platelet numbers increase markedly within 3–5 days of vincristine administration, and the addition of vincristine to standard therapy in dogs with IMT appears to shorten hospitalization time by several days. Most authors currently recommend an intravenous vincristine bolus dose of 0.02 mg/kg for the treatment of canine IMT. Vincristine has been used in cats with IMT, although evidence of clinical efficacy is lacking. One significant advantage of vincristine compared to other therapeutic options for IMT is that vincristine is inexpensive (a 1-ml vial of 1mg/ml vincristine sulfate costs around $20).

Neurotoxicity, although uncommon, is the most frequent significant side effect associated with therapeutic doses of vincristine in dogs and cats.

The pathogenesis of vincristine-induced platelet responses in IMT patients is uncertain. Studies in people suggest that the main therapeutic effect of vincristine in IMT patients is not increased thrombopoiesis. Post-treatment average platelet lifespans are significantly prolonged in patients that respond to vincristine, suggesting that remission is due to reduced platelet destruction rather than increased platelet production. Since platelets are the major circulating cellular carriers of vincristine, researchers have speculated that antibody-coated platelets selectively deliver vincristine to those phagocytes within the mononuclear phagocytic system that are actively involved in platelet destruction. This proposed mechanism explains why, despite being an ineffective immunosuppressive agent for the treatment of most conditions, vincristine can still be very effective for the treatment of IMT.

Neurotoxicity, although uncommon, is the most frequent significant side effect associated with therapeutic doses of vincristine in dogs and cats. Reversible vincristine-induced neurotoxicity in the dog has been reported with chronic cancer chemotherapy, but is not likely to be an issue with the single doses used to treat IMT. Other side effects such as GI disorders and alopecia, occur less frequently, and are typically mild and temporary. Vincristine at doses used for IMT typically causes minimal myelosuppression in dogs, although dogs with the ABCB1-1Δ (MDR1) gene mutation and some Border Collies have been reported to be more susceptible than other dog breeds to myelosuppression at antineoplastic vincristine doses. An unusual transient pulmonary toxicity has been reported in a cat receiving chemotherapeutic doses of vincristine. ❑

Leptospirosis

Meredith von Roedern, DVM, DACVECC

Pathophysiology:

▪ Leptospirosis is caused by a motile spirochete bacterium. Leptospirosis has a worldwide distribution and the incidence of leptospirosis has increased in recent years. In the US, Leptospirosis is wide spread with particularly high prevalence on the East Coast, West Coast and in the Southwest. Leptospirosis can cause significant morbidity and mortality in affected dogs and is also zoonotic. Leptospirosis is transmitted via urine and spread via contact with intact mucous membranes and/or open wounds. It is carried in the urine of 150+ mammals including rodents and can live in soil for several months.

Leptospirosis has a worldwide distribution and the incidence of leptospirosis has increased in recent years.

Clinical signs/diagnostic findings:

▪ Clinical signs can be variable and may include: Fever, lethargy, anorexia, vomiting, diarrhea, abdominal pain, muscle pain and stiffness, icterus, tachypnea/dyspnea, coughing, hematuria, PU/PD or oligoanuria, and uveitis

▪ Diagnostic testing may show any of the following abnormalities (absence of any of these findings does not rule out leptospirosis)

- ✔ **CBC:** Neutrophilia +/- left shift, thrombocytopenia, anemia, lymphopenia
- ✔ **Biochemical profile:** Azotemia, liver enzyme elevation, hyperbilirubinemia, electrolyte changes, increased CK
- ✔ **UA:** Isothenuria/hyposthenuria, proteinuria, glucosuria, hematuria, pyuria, casts, bilirubinuria
- ✔ **PT/PTT:** may be prolonged
- ✔ **Thoracic radiographs:** Diffuse to nodular interstitial to alveolar pulmonary pattern (Leptospirosis has been associated with a syndrome of pulmonary hemorrhage in some cases) – See **figure 1**
- ✔ **Abdominal ultrasound:** Non-specific – renomegaly, ascites, pyelectasia, medullary band of increased echogenicity or increased cortical echogenicity, pancreatitis

Testing

Any animal with an acute kidney injury (AKI) or acute on chronic kidney injury should be tested for leptospirosis, and testing may be indicated in any animal with compatible clinical signs. Testing for leptospirosis is unfortunately somewhat complicated.

▪ *PCR Testing* – PCR testing can be performed on urine and/or blood and detects leptospira DNA – This test has good specificity, but only variable sensitivity (risk of false negative). This test is best used early in the course of disease and samples should be collected prior to antibiotic administration. Submitting both blood and urine may increase the sensitivity of the test. If the PCR comes back positive, this generally indicates current active infection. If the test comes back negative, additional testing is needed to completely rule out leptospirosis. This test may confirm leptospirosis earlier in the course of disease than waiting for serology/seroconversion.

▪ *MAT testing:* Microscopic agglutination test measures serum antibodies to several leptospirosis serovars. The MAT may be falsely negative early in disease because the patient may not have had enough time to mount an antibody response. Additionally, the MAT could be positive due to vaccination or previous exposure and does not necessarily indicate an active infection. For this reason, acute and convalescent titers (initial sample and then repeat sample taken 1-2 weeks later) are necessary to make a definitive diagnosis. A four-fold increase in titers taken 1-2 weeks apart is the gold standard for the diagnosis of leptospirosis in dogs.

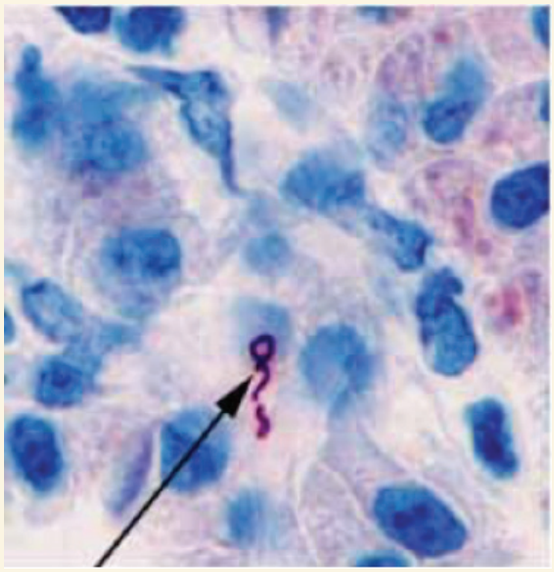

Figure 1. *Leptospirosis Spirochete in Kidney Tissue*

▪ *SNAP Lepto (IDEXX) and WITNESS® Lepto (Zoetis):* Both of these tests are antibody tests that can be performed rapidly in clinic, however, because the tests measure serum antibodies, they may be falsely negative early in course of disease and may be falsely positive secondary to vaccination or previous exposure.

▪ I prefer to submit Lepto PCR and acute and convalescent MATs as I feel that this gives me the best chance of rapid diagnosis (PCR) in many cases, while decreasing the chances of false negatives (acute and convalescent serology).

Treatment:

▪ Doxycycline is the treatment of choice for treatment of leptospirosis. The ACVIM consensus statement recommends 5mg/kg IV or PO BID for 2 weeks. Ampicillin can be used at 20mg/kg IV q6 in dogs that initially cannot tolerate doxycycline, however, doxycycline should be administered for 2 weeks following resolution of GI signs to prevent renal carriage. Azotemic or dehydrated patients should be treated with IV fluids with careful serial assessment of hydration and volume status. IV fluid therapy needs to be tailored to the patient because some patients with leptospirosis will develop oliguria/anuria and can become severely overhydrated with IV fluid therapy and other patients will be profoundly polyuric and can become very dehydrated despite aggressive IV fluids. Signs of fluid overload include chemosis, serous nasal discharge, increased skin turgor, peripheral edema, abdominal or pleural effusion, tachypnea and crackles. The patient body weight should be monitored often (q6-q12h). Significant increase in body weight beyond what is

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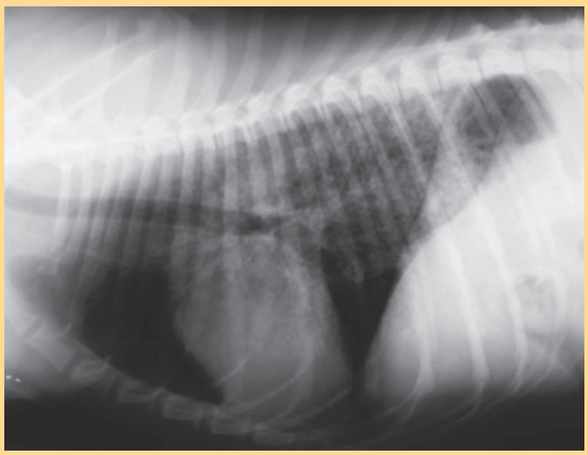
Leptospirosis

➤ *Continued from Page 9*

deemed appropriate to account for apparent level of dehydration, warrants re-evaluation for fluid overload. Urine output monitoring via indwelling urinary catheter, if available, can be used to assess for both oligoanuria and polyuria and can be used to more accurately tailor fluid therapy to the patient's fluid needs. For patients with signs of oligoanuria and overhydration, referral for dialysis should be considered if possible as prognosis with dialysis in the management of leptospirosis associated AKI is reported to be as high as 86%.

Figure 2. *Lateral thoracic radiograph of a dog with leptospiros showing a generalized severe reticulonodular interstitial lung pattern with patchy alveolar consolidations – consistent with the syndrome of pulmonary hemorrhage.*



Prevention:

▪ Vaccination markedly reduces the chances of developing clinical signs associated with leptospirosis as well as markedly decreasing the renal shedding of leptospirosis after challenge. Although AAHA lists the lepto vaccine as non-core to be given to "at-risk" patients, I strongly recommend vaccination in all dogs, including dogs that are indoor only. Because rodents can carry and transmit leptospirosis, outdoor exposure is not necessary for the development of leptospirosis. Recently, a large majority of my leptospirosis positive cases have been in small breed urban dogs with minimal outdoor exposure – likely because these dogs have not been vaccinated due to low perceived risk. Leptospirosis infection can be associated with high morbidity and mortality in addition to the zoonotic risk; for this reason, vaccination in all dogs should be strongly considered. The leptospirosis vaccine can be started as early as 8-9 weeks of age. The initial vaccination requires the administration of 2 doses given 2-4 weeks apart. Following initial vaccination, dogs should be re-vaccinated every year.

Highlights

▪ Leptospirosis is common and diagnosis is increasing in frequency over time

▪ Patients are at risk of leptospirosis even if they are primarily or exclusively housed indoors

▪ Vaccination should be strongly considered in ALL dogs every year

▪ All dogs with acute kidney injury, acute on chronic kidney injury or other signs compatible with leptospirosis should be tested for leptospirosis, ideally using a combination of PCR and acute and convalescent serology

▪ Dialysis can be used to manage patients that develop oligoanuria and overhydration with standard IV fluid therapy and prognosis with dialysis can be favorable if clients have the financial resources. ❑

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If the dog:

- Is taking medications for seizures or "epilepsy"
- Had its first seizure between 6 months to 6 years of age
- Weighs between 25 and 110 pounds
- And continues to have seizures while on medication.....

then the dog might be eligible to participate in the **Fully Funded** Clinical Epilepsy Study at Long Island Veterinary Specialists. A new treatment is under investigation and if enrolled, all care is free for qualified participants.

Contact Dr. Dominic J. Marino or Dr. Patrick Roynard at 516-501-1700 or email epilepsystudy@livs.org for more information on a new treatment option.

Epilepsy Clinical Trial Team

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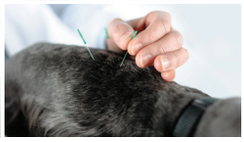

To refer your clients to Dr. Selmer, call
516-501-1700 or visit www.livs.org

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Dr. Michel Selmer is an Integrative Veterinarian and one of only a handful of Traditional Chinese Veterinary Medicine Practitioners that holds a Master's Degree in the United States.

Dr. Selmer is a certified TCVM practitioner and provides the following Integrative Medical Therapies:

- Veterinary Acupuncture
- Herbal Medicine
- Veterinary Food Therapy
- Veterinary Tui-na

To learn more about Dr. Selmer and Traditional Chinese Veterinary Medicine, check out his book: ***"The Best of Both Worlds, An Advanced Guide to Integrative Veterinary Care for Healthier, Happier Pups"***