# Central Connection

**Your Connection to Valley Central - SPRING 2015**

## IN THIS ISSUE:



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# Leaders in Specialty Care

Dear Colleagues:

Welcome to our Spring 2015 newsletter. In this issue, we have included articles written by Dr. Mary Landis , Dr. Stacey Dietrich, Dr. Craig A Clifford, and Kacee Cope, CVT.

Our commitment is to keep you and our clients updated on medical topics and new services offered at Valley Central Veterinary Referral and Emergency Center. The doctors and staff at Valley Central Veterinary Referral and Emergency Center want to thank you for your sustained and continued support. Our continued goal is to provide the highest standard of veterinary care for your clients. We understand that our success as a referral hospital is a result of your confidence in the veterinary service we provide for your clients and patients. Please do not hesitate to contact any doctor or staff member with questions or concerns regarding any aspect of our veterinary hospital services.

Allyson Tolliver, Hospital Administrator

## Updates From VCVREC:

*Save a Paw Foundation*

We are happy to announce we have partnered with the Veterinary Care Foundation to create **Save a Paw Foundation** to provide another financial resource for animals in need of specialty veterinary care. VCVREC donates thousands of dollars in financial assistance each year to regional rescue organizations, abandoned animals and owners experiencing financial hardship. Save a Paw will allow us to optimize the generous donations of our clients and animal advocates through the use of a charitable 501(c)3 fund. Through this Foundation we will be able to provide small grants on an as-needed basis to pets qualifying for our program.

VCVREC patients considered candidates for a Save a Paw Foundation grant would include the following:

- Helping fund a Good Samaritan case
- Assisting owners that are in a financial crisis

Funding recipients must have a treatment plan and estimate from VCVREC and demonstrate that all other payment options have been exhausted including:

- Personal finances (credit cards and care credit)
- Donations from family and friends
- Additional fundraising efforts

Anyone can make a donation to Save a Paw through our secure on-line process or send a check made payable to The Veterinary Care Foundation (Memo Valley Central Veterinary Referral and Emergency Center) and send to 16550 NW 46th St., Morriston, FL 32668. Your gift to Save a Paw is tax-deductible and 100% of your gift will go to supporting the care of pets in need. Every dollar helps us save animals one paw at time.

We are also happy to announce that Advanced Veterinary Imaging of the Lehigh Valley is coming early summer. We will have the Vimago™, which will be the only Robotic, High Definition, Computed Tomography-Fluoroscopy system in the area made by Epica Med, a veterinary company. The unit is a low-dose radiation system. The trend has been to try and get away from high-dose radiation exposure. Human medicine will closely be following suit. The system operates at a speed equivalent to a 4-slice conventional CT with 3-D reconstruction software capabilities. Images can be exported as DICOM and viewed by any adequate DICOM viewing software. The Vimago™ can also be used as a diagnostic or interventional Multi-modality imaging device. The Vimago™ will have the capabilities to perform Robotic planning with placement of accurate total hip prostheses components and other implant devices. The Vimago™ also adequately images all aspects of the nervous system including the brain. Advanced Veterinary Imaging of the Lehigh Valley will serve the entire veterinary community. It has been a complicated task and very time consuming for clients and pets to travel long distances for various imaging modalities.

Mary Landis, V.M.D., M.A. (Ophthalmology)

# Keratoconjunctivitis Sicca (KCS) and other Tear Film Abnormalities

Keratoconjunctivitis sicca (KCS) results from inadequate production of one or more of the three components of the tear film and is one of the more common conditions encountered in dogs and cats. The avascular cornea, like all living tissues, requires oxygen and nutrients. It is dependent upon a healthy tear film. The outer most layer consists of primarily lipid which minimizes evaporation. This lipid layer is secreted by the meibomian glands in the eyelids. The middle layer is aqueous and is produced by the lacrimal glands. These glands are located in the upper eyelid and in the third eyelid. This is the thickest of the layers and the most important in maintaining metabolic homeostasis. The inner most mucoid layer of the tear film is secreted by the conjunctival goblet cells and spreads across the epithelial surface to increase surface tension and optimize distribution of the aqueous layer.

Inadequate production of the aqueous component is the most common cause of KCS and induces the most dramatic tissue response. Acute aqueous insufficiency can result in marked discomfort, corneal ulceration and perforation. The undiluted mucoid component forms a characteristic thick and adherent discharge. As a response to the loss of the aqueous tear film, the cornea will transform to have characteristics of epidermal tissue with pigmentation, vascularization and scarring. A result of this protective mechanism, the cornea will have a loss of transparency and deleterious effects on vision. Deficiencies in the mucinous or lipid layers result in less dramatic but similar chronic, non-specific signs of ocular surface irritation.

## DIAGNOSIS OF KCS

Diagnosis is based on history, clinical signs and a number of diagnostic procedures including: the Schirmer Tear Testing (STT) which measures aqueous tear production (normal 10-20mm/min in dogs, lower in cats); tear film break-up time as determined with fluorescein dye (normally > 60 sec in dogs and cats) and vital staining of the corneoconjunctival epithelium special stains. These tests provide insight into mucinous and lipid elements of the tear film.

5-year-old Westy with KCS. STT 0. Crusting of exudate on lids and thick mucoid discharge adherent to the ocular surface. The cornea is scarred and pigmented.

## CAUSES OF KCS

A number of causes have been documented for KCS including hypothyroidism; infectious lacrimal adenitis (viral induced), immune-mediated disease which destroys the tear secreting glands; and neurogenic disease. Sulfa-containing antibiotics and non-steroidal anti-inflammatory drugs may result in either reversible or irreversible KCS. Topical parasympatholytics (atropine) will decrease tear production physiologically.

## TREATMENT OF KCS

There are several considerations for treating keratoconjunctivitis sicca. The dry eye patient frequently has a buildup of mucoid discharge which may itself be irritating and serves as a media for bacterial growth. Aggressive irrigation with a saline eyewash is recommended at least twice daily. The use of treatment of topical lacrimostimulants including immunomodulating agents such as cyclosporine (Optimmune) and tacrolimus. These medications represent one of the most important advances in veterinary ophthalmology. Used twice daily they stimulate a patient's aqueous tear production. Approximately 75-80% of patients may be managed medically using these drugs. Local irritation is the most common side effect, occurring in 5% of patients. Many patients will usually respond to changing vehicle or

## Keratoconjunctivitis Sicca (continued)

agent. These drugs demonstrate a dose response and are synergistic for managing refractory cases.

Neurogenic cases, diagnosed when dry eye is accompanied by ipsilateral crusting of the external nares (the glands in the nasal mucosa are affected as well), may respond to the addition of oral or topical pilocarpine.

Lubricants are utilized on a regular schedule with frequency determined by the severity of tear depletion. Generally the greater the viscosity the better; we prefer Genteal, Systane, or Optixcare plus hyaluron, given hourly in absolute KCS or 4 times daily in cases of suspected mucus or lipid deficiency. It is important to note that we have been impressed of the benefits of including hyaluronic acid in the treatment regimen.

The medical treatment of dry eye syndrome is usually a life-long undertaking. The education of the client is critical. Compliance to the diligent care of the pets' eyes by owners is key in achieving the management goals of patient comfort and preventing progression of potentially blinding surface disease.

The final therapeutic option to mention is the parotid duct transposition. This is a surgical procedure with varying degrees of success. Complications can be challenging to manage.

**The take home points for managing KCS are:**

1. KCS is a common disease among dogs and cats.
2. There are different forms of KCS and therapy is targeted at the specific problem.
3. There are different forms of therapy; including medical and surgical options.
4. If left untreated or poorly managed, blinding corneal disease will occur.
5. Owner compliance is critical.

# EMERGENCY MEDICINE

By: Stacey Dietrich D.V.M. (Emergency Medicine)

## Acute Trauma

A recent conversation with a colleague concenrned an 8-year-old Golden Retriever who was hit by a car. I know how daunting these cases can be, especially since they are infrequent and usually very critical, so let's review the pertinent questions.

1. **The dog has lung changes on x-rays and is having some difficulties breathing. Can I give Lasix to get the fluid out of the lungs?**

I asked if the dog ever had a history of congestive heart failure or if the heart was enlarged on x-rays. He said there was no history of this, but wanted to know what the treatment was to get the fluid out of the lungs. I told him that the "fluid" in the lungs was likely as a result of contusions. The contusions can worsen over the next 72 hours, just as a bruise on your skin worsens in time. It is important to give nasal oxygen, especially if he is having difficulties breathing, until he can breathe normally on regular air. In the case of shock, flow-by oxygen is one of the most important things to do on presentation to prevent the formation of lactic acid from anaerobic metabolism of the cells.

2. **The dog does not appear to be in shock at all, can this be possible?**

Early on in compensatory shock, these patients can look deceivingly normal. Therefore, it is very important to assess his vitals, including mucous membrane color and CRT, heart rate, respiratory rate, and blood pressure. This patient's mucous membranes were white. He also had a fast heart rate and respiratory rate, but my mentor

thought this was due to pain. He did not take a blood pressure on the patient yet, but the PCV/TS was 38%/4.0.

Based on the above information, this patient is definitely in hypovolemic shock from internal bleeding. It is likely that he is bleeding from trauma to the spleen/liver, however, the bleeding into his lungs could also be a contributing factor. In patients with acute hemorrhage, often the PCV will be normal initially, but the TS will be low. Therefore, it is very important to check a PCV with a TS and evaluate them together.

After giving oxygen, in patients with hypovolemic shock, it is important to give boluses of IV fluids to help restore blood volume and resultant blood pressure. In dogs, I typically will give 15 mL/kg boluses over 15 minutes and reevaluate blood pressure, mucous membranes, heart rate, and respiratory rate after the boluses are complete. Well-balanced isotonic solutions such as Normosol-R, Plasmalyte, or Lactated Ringer's Solution are typically used for boluses. In cases of severe shock, I will sometimes add a colloid such as hetastarch at boluses of 5 mL/kg. After the patient is stable, I will often continue with the remaining amount of daily hetastarch for the patient, divided by 24 hours. When using colloids, it is important that an adequate amount of crystalloids have been given, in order for these agents to work effectively. In addition, repeat blood pressures are helpful with patients receiving colloids to make sure they are getting enough, but not too much, of this therapy.

3. **Should I give steroids to this dog to help with his shock?**

In the past, steroids were often used as a treatment for hypovolemic shock, however, this has fallen out of favor. Unfortunately, studies have shown that steroids do little to help with shock, but definitely can cause adverse effects such as hyperglycemia, immunosuppression, gastrointestinal ulceration, and decreased healing times. In some cases, the use of steroids in shock has actually been associated with increased mortality.

At the end of the conversation, I realized that the above questions have been asked repeatedly by practitioners and are good to think about when dealing with any case of acute trauma. It is important to note, however, that the status of the patient can change very quickly during these types of emergencies. Therefore, close monitoring and rapid changes in the treatment regimen are key for the patient's survival.

## ONCOLOGY

By: Dr. Craig A Clifford D.V.M., M.S., D.A.C.V.I.M. (Oncology)

# Canine Lymphoma: A New Hope

Traditionally, all lymphomas were deemed the same and treatment was a simple recipe with "one size fits all" for therapy. With the advent of newer immunologic, molecular and histologic diagnostics, the treatment of lymphoma is changing. Currently, decisions regarding which chemotherapeutic agents/protocols to be utilized is now based upon tumor grade, location, histologic subtype and phenotype.

On a very basic level, lymphoma is broken down into two main phenotypes, B and T cell. Traditionally 2/3 of dogs with lymphoma are classified as B cell and 1/3 are T cell. A minor percentage (<2%) are deemed "null cell." Phenotyping of lymphoma patients can be achieved through a variety of tests including immunohistochemistry, immunocytochemistry, PARR and flow cytometry.

a. Immunohistochemistry (IHC): IHC is still considered the "gold standard for determining phenotype utilizing a panel of markers that bind to surface proteins either on B cells (cd79a, cd21, Pax5) or T cells (cd5, cd3, cd,4, cd8). This requires tissue obtained either via a punch biopsy, tru-cut biopsy, or nodal extirpation

b. Immunocytochemistry (ICC): ICC utilizes the same antibodies as IHC but on cytology samples thus offering a more cost effective manner to obtain phenotype. The distinction is that nodal architecture is not evaluated thus specific subtypes of lymphoma cannot be determined.

c. Polymerase Chain Reaction (PCR): This is a repetitive enzymatic reaction that generates ~$10^9$ copies of a particular DNA sequence from 1 original copy, thus a small sample can yield results. It utilizes heat-stable polymerases and sequence specific primers. This test is commonly used in the identification of infectious disease in human and veterinary medicine. PCR for antigen receptor rearrangement (PARR): Clonality is the hallmark of malignancy, and PARR amplifies the variable regions of immunoglobulin genes and T-cell receptor genes to detect the presence of a clonal population. PARR not only determines clonality (cancer) but will also determine the phenotype of lymphoma or lymphoid leukemias. Specific sites/samples that can be analyzed include: lymph node or mediastinal mass aspiration, body cavity fluids, cerebral spinal fluid, bone marrow or peripheral blood.

d. Flow Cytometry (FCM): FCM is routinely used in human medicine early in the work-up of lymphoid malignancies and involves the use of monoclonal antibodies + fluorescent markers. This allows the evaluation of a large number of cells to determine differences in cell size (small vs. large), phenotype of circulating atypical cells and presence of aberrant surface marker expression. FCM requires fresh samples of blood or tissue (lymph node, mediastinal mass) and is commercially available through major diagnostic laboratories.

T cell lymphoma is more commonly associated with certain breeds including the boxer, golden retriever, Australian shepherd, Asian lap dogs and Siberian husky. T cell LSA is also associated with certain anatomic forms including cutaneous (epitheliotropic, AKA ELSA), mediastinal, hepatic and gastrointestinal. Many studies have documented a worse prognosis for dogs with T-cell lymphoma and for this reason, many oncologists have begun modifying protocols based upon phenotype. Further support of this was based upon a retrospective study in which the response of T cell LSA to a single dose of doxorubicin was ~50% vs ~100% for dogs with B cell LSA. The discussion was then raised to include more alkylating agents into T cell protocols based upon evidence of high responses in dogs with ELSA treated with lomustine (CCNU). Although, only 17% experienced a complete remission (CR), 61% experienced a partial remission (PR). The combination of L-asparagine, mechlorethamine, vincristine, procarbazine, and prednisone (L-MOPP) has been investigated in dogs with T-cell lymphoma. Overall, L-MOPP protocol was associated with a complete remission rate of 78%, and overall survival 270 days, However, >20% were alive at >900 days. The challenge with this protocol is cost, difficulty of administration and toxicity. Currently protocols with substitutions of CCNU for doxorubicin and Elspar in each cycle are underway and are standard at this author's practice.

**Novel LSA Therapy:**

***Chemotherapy: Tanovea™*** was discovered by Gilead Sciences, Inc., and licensed to VetDC (http://vet-dc.com/) for use in animal cancer, (previously known as VDC-1101) was designed to preferentially target and attack cancer cells implicated in lymphoma. In previous clinical studies, Tanovea™ has been shown to be highly effective with a 77% overall response rate. Tanovea™ was generally well-tolerated and demonstrated high rates of response in both dogs naïve to previous treatments as well as in dogs that relapsed or failed previous chemotherapy. Tanovea is administered IV on a 3 week schedule and large scale studies are underway. The goal of this study is to evaluate the effectiveness of TanoveaTM in naive or relapse lymphoma patients. The class of drug is unlike any in our current standard chemotherapy protocols thus offers the first new LSA drug in many years and preliminary results are promising. A clinical trial evaluating Tanovea is ongoing at Hope Veterinary Specialists (www.HopeVS.com).

***Monoclonal antibody therapy:*** A monoclonal antibody (mAb) can be used to specifically bind to target cells or proteins. This may then stimulate the patient's immune system to attack those targeted cells and remove them from the body. In human oncology, monoclonal antibodies have been developed for T

# Canine Lymphoma: A New Hope (continued)

and B cell Lymphoma which allows the immune system to recognize, attack and remove them. Normal lymphocytes cell can be replenished, as stem cells within the bone marrow are not targeted and as such normal cells are replenished but the cancer lymphocytes are not. These have now become standard of care therapy in human oncology. Cancer cell killing is thought to be via three mechanisms:

- Antibody-dependent cellular cytotoxicity (ADCC)
- Complement-mediated cytotoxicity (CMC)
- Induction of apoptosis (natural cell death)

Two distinctly different veterinary monoclonal antibodies are available for dogs with T cell (conditional approval by USDA; Aratana: http://www.aratana.com/) and B cell (full approval by USDA; Novartis/Elanco). To date they have been shown to be safe and have a reasonable expectation of efficacy. Each are being evaluated in separate large scale trials (www.vetcancertrials.org) along with standard chemotherapy. If similar efficacy to their "human" counterparts is noted, they will become standard of care in veterinary medicine and further pointing toward the necessity to phenotype all LSA patients.

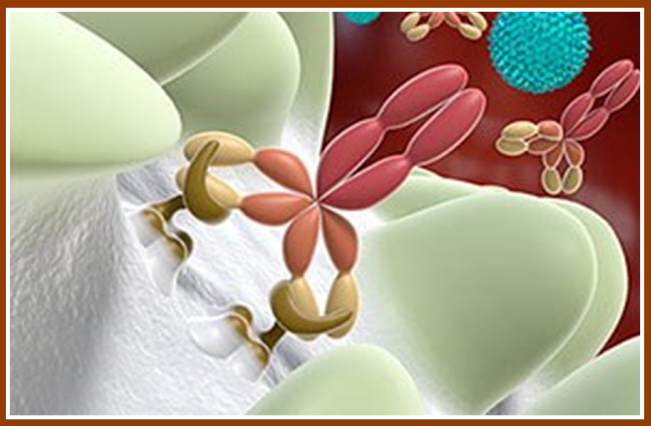

Figure 1: a monoclonal antibody binding to its receptor on the surface of a lymphoma cell.

For a video displaying the mechanisms of action of a monoclonal antibody: http://aratana.com/therapeutics/pipeline/cancer

We currently have the T cell monoclonal antibody and thus the ability to add this to our arsenal of treatments options for dogs with T cell lymphoma. This includes naïve/relapse as well as gastrointestinal, mediastinal and cutaneous lymphoma. For more information regarding the schedule of treatments. Please contact our office for more information regarding this novel and exciting therapy.

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NURSES TIP

By: Kacee Cope, C.V.T.

# Limb Amputations in Pets: Who needs 4 legs anyway?

Amputation is one of the scariest words that a pet owner can hear; it often causes grief, heartache and trauma in the minds of the owner. Helping owners to understand the recovery from this surgery can give some hope for the weeks follow and ease the mind in making the best decision for their pet.

Amputation is most common after severe trauma or neoplasia involving skin and/or bone. Post operative recovery will include sufficient pain medications, antibiotics and sling support if necessary. Activity restriction is recommended for two weeks to allow proper healing of skin and allow the animal to learn their new balance, but most recovery is unremarkable. After about a week most animals have returned to a completely normal functioning life, and mobility is very rarely compromised. Unlike humans, animals rarely suffer any physiological trauma from losing the limb which allows their recovery to be so rapid.

Good weight management and joint supplements to keep all remaining joints healthy will only further the quality of life for the pet. In cases where mobility does become compromised pet wheelchairs and/or orthotics can also help aid the pet for a continued good quality of life.

Pets with limb amputations have gone on to live completely normal and happy lives. In fact as humans we should marvel at their bravery and strength.

VALLEY CENTRAL
VETERINARY REFERRAL AND EMERGENCY CENTER

210 Fullerton Avenue
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VCVREC, serving the Lehigh Valley and surrounding areas since 1996, is dedicated to providing state-of-the-art veterinary care for your patients.

## Specialists at Valley Central Veterinary Referral and Emergency Center

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