

Central Connection

Your Connection to Valley Central - SPRING 2013



Leaders in Specialty Care

Dear Colleagues:

Welcome to our Spring 2013 newsletter. In this issue, we have included articles written by Dr. Craig A. Clifford, Dr. Robert Peiffer and Angie Itterly, CVT.

Our commitment is to keep you and our clients updated on medical topics and new services offered at Valley Central Veterinary Referral Center. The doctors and staff at Valley Central Veterinary Referral 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

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Updates From VCVRC:

Oncology Services are Now Available at VCVRC.

We are very pleased to announce Dr. Craig Clifford and Dr. Kate Vickery have joined our practice.

Dr. Clifford received his DVM from Mississippi State University in 1999. He subsequently completed his internship in small animal medicine & surgery and his residency in oncology at the University of Pennsylvania.

He has been a fellowship examiner for the Australian College of Veterinary Scientist, a member of the ACVIM residency training and credentials committee, a member of the Veterinary Cancer Society Executive Board & Founder of the VCS Residency Review Session at the annual meeting, a consultant to the Veterinary Information Network, Animal Clinical Investigations Network, Novartis Animal Health, Pfizer, Oasmia Pharmaceuticals, BoehringerIngelheim, Pet Medicus Laboratories, and AB Science. Dr Clifford is also an advisory board member of the Animal Cancer Foundation which provides support for funding translation research. A Co-Founder of the Northeastern Veterinary Co-operative Oncology Group.

Dr. Vickery majored in Molecular Genetics and Biology and earned a Bachelor of Science degree from King's College, Wilkes-Barre. She

is a graduate of the University of Pennsylvania, School of Veterinary Medicine. After obtaining her VMD degree, she went on to complete a three-year combined Residency and Master's Degree in Medical Oncology and Cancer Biology at the world renown, Animal Cancer Center at Colorado State University.

Dr. Vickery has published research articles in Veterinary Comparative Oncology and Journal of Veterinary Internal Medicine, peer reviewed journals. She is an active collaborator for clinical trials sponsored by numerous veterinary universities, pharmaceutical companies and Animal Clinical Investigations Network. She has lectured nationally to veterinarians and veterinary students on the topic of Veterinary Oncology. Dr Vickery holds the position of Chair of the Oncology Forum Planning Committee for the American College of Veterinary Internal Medicine. She is a member of the Veterinary Cancer Society, American College of Veterinary Internal Medicine, and the American Veterinary Medical Association.

Our Oncologists strive to provide the highest quality patient care and client service. Client education and recognition of the human-animal bond are both imperative in their daily practice. Dr. Clifford and Dr. Vickery's schedule consist of seeing patients Tuesdays and Thursdays. To refer a patient to our Oncology Department please have your client(s) call 610-435-1553.



OPHTHALMOLOGY

Robert Peiffer, D.V.M., Ph.D., D.A.C.V.O.

Canine Indolent Ulcers (SCCEDs - Superficial chronic corneal epithelial defects)

Indolent ulcers, also known as Boxer ulcers, recurrent epithelial erosions, or SCCED, are common in middle to older aged dogs of all breeds but most commonly, as one might suspect, Boxers. Pathogenesis is thought to involve a defect in stromal-epithelial adhesion; sliding with blinking and eye movement causes the epithelium to break down with resultant superficial ulceration and the inability of the epithelium to adhere to the underlying stroma results in abortive and prolonged healing. More often than not a history of precipitating trauma cannot be elicited and the majority occur spontaneously.

Diagnosis of an indolent ulcer is made by the following characteristics:

- Signalment
- History of a similar prior problem, frequently with evidence of mild corneal scarring, as well as chronicity of the current problem (an uncomplicated superficial ulcer will heal in a week or less)
- The great majority are unilateral, with bilateral cases uncommon
- Variable but usually notable discomfort, as manifested by blepharospasm
- Conjunctival injection, with serous to seromucoid discharge, and frequently with protrusion of the third eyelid
- Corneal epithelial defect with a marginal lip of non-adherent epithelium that easily is removed with a cotton applicator (healthy epithelium will remain upon gentle rubbing). Fluorescein dye will facilitate visualization of the non-adherent epithelium and magnification (ideally with a biomicroscope) assists diagnosis. Edema of the adjacent stroma is variably present; while the center of the cornea is most commonly involved, peripheral and/or multiple lesions may be encountered (Fig 1).
- Absence of infection, as evidenced by lack of stromal infiltrate
- Limbal neovascularization may or may not be present; if seen it is a favorable prognosticator of imminent healing. Exuberant vascularization and granulation are a common component of the healing process.

It is critical to accurately assess the cornea for any evidence of infiltrate or infection and to determine depth of the

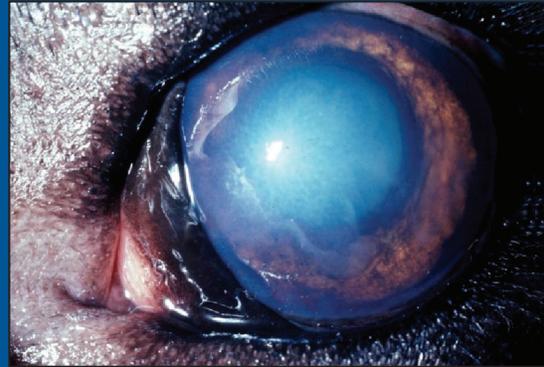


Figure 1: Large central indolent ulcer; note shallow depth, non-adherent margins, absence of infiltrate, and associated stromal edema

corneal defect to make the diagnosis of an indolent ulcer. Anything other than a purely epithelial defect, or an infected ulcer, requires more aggressive medical management and/or surgical management. Keratotomy and debridement are contra indicated in deep or infected ulcers, nor in cats where the procedure may precipitate sequestration.

The mechanism(s) by which keratotomy aids epithelial re-attachment is not well-understood; it may be as simple as providing an irregular scaffold for the sliding epithelial cells to latch onto. Trauma to the stroma may release cytokines that stimulate healing or allow keratocyte migration into the subepithelial space to produce binding fibrosis (Fig 2).

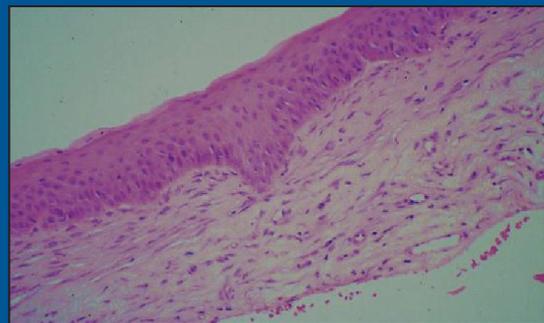


Figure 2: Keratotomy following punctate keratotomy with an epithelial facet at the keratotomy site with adhering subepithelial fibrosis and stromal vascularization.



OPHTHALMOLOGY

Robert Peiffer, D.V.M., Ph.D., D.A.C.V.O.

Canine Indolent Ulcers (continued)

In cases of indolent ulceration, the cornea is unlikely to heal without intervention. Debridement of the non-adherent corneal edges can be performed after instillation of topical anesthesia with proparacaine. A cotton tipped swab is used to gently remove all of the loose epithelium surrounding the corneal ulcer which will usually greatly increase the size of the defect. After debridement, shallow wounds can be made in the underlying superficial stroma a grid or punctate fashion using a 22-25 g hypodermic needle. Alternatively a diamond burr debridement can be performed. We prefer the punctate keratotomy because it is the easiest and safest to perform, can be carried into adjacent adherent epithelium, and produces the least scarring. A soft contact bandage lenses are applied after debridement and keratotomy to improve comfort and aid in healing.

We prefer Bausch and Lomb plano (no refractive power) bandage lenses, which fit most of our patients reasonable well; lenses specifically made for animals are available but in general more expensive. The lenses stabilize and protect the healing epithelium and provide comfort to the patient. In about 50% of cases the lens is retained until recheck where they are readily removed with a drop of topical anesthesia and a cotton applicator. Alternatively they may be blinked out almost as the patient leaves the office, or anytime between placement and recheck. The pet owner may not know if the contact has been retained or not. It seems that they are required for only a few days for salutary effect and we will replace them only if marked discomfort returns.

Medical management includes prophylactic antibiotic treatment with a first line topical solution (Neopolygram, tobramycin, gentamicin); once or twice daily is effective in preventing secondary infection. Stronger fluoroquinolones should be reserved for cases of corneal infection. Atropine is usually not necessary in cases of indolent ulceration if the pupil is not miotic. Our philosophy is one of minimalism in treatment, the objective being to create an optimal environment where the cornea can heal itself. Atropine decreases tear production and thus may be a detriment to healing. Discomfort is almost always ameliorated with the contact lens. Serum and other purported facilitators of healing are neither required nor beneficial. Ointments retard healing

more than solutions and are less compatible with the soft contact lens.

85% of indolent ulcers treated as above will heal within 7-10 days; resolution of blepharospasm is a reliable indicator of progressive healing. Once the defect has epithelialized and is fluorescein negative a short course of topical steroids will minimize vascularization with a resultant slight superficial corneal scar that does not compromise vision. If resolution has not occurred at recheck the process is repeated. After 3 attempts with less than satisfactory results a lamellar keratectomy is performed and is almost always curative (Fig 3).

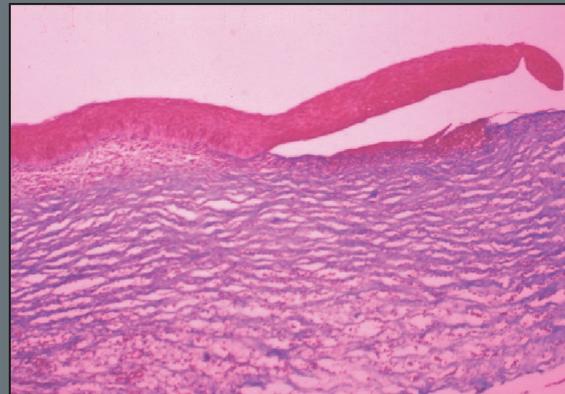


Figure 3: Keratectomy specimen from a dog. Refractory to multiple debridement/keratotomy/soft contact Procedures. The non-adherent marginal epithelium is characteristic.

Cats may present with ulcers that mimic indolent ulcers clinically; underlying FHV-1 infection or early sequestrum should be considered in the differential diagnosis. Management of suspected indolent ulcers includes debridement with a cotton applicator soaked in dilute povidone iodine solution, a contact bandage lens, and prophylactic topical antibiotic solutions.

In our experience future recurrence in the same or fellow eye occurs approximately 50% of the time and client education in this regard should be a component of the management strategy.



ONCOLOGY

Craig A. Clifford DVM, MS, DACVIM (Oncology)

What's New in Veterinary Oncology: Novel Diagnostics and Tyrosine Kinase Inhibitors

Novel Diagnostics: With the advent of newer technology and better veterinary platforms, novel diagnostics are becoming more commonplace for the oncology and general practitioner.

Polymerase Chain Reaction (PCR): This is a repetitive enzymatic reaction that generates ~10⁹ 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. Other applications include the identification of kit mutations within mast cell tumors (MCTs) performed from either aspirate or histopathology samples. This test can be performed as a “stand alone” or as part of a MCT panel (www.dcpah.msu.edu/Sections/Immunohistochemistry/FAQ.php#08). Identification of the mutation is important in the prognosis and provides a logical basis to the addition of a tyrosine kinase inhibitors.

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, cavity fluids, cerebral spinal fluid, bone marrow or peripheral blood.

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 cells 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.

Tyrosine kinases and their inhibitors: Receptor tyrosine kinases (RTKs) are cell-surface receptors for extracellular growth factors that facilitate signaling to the cell interior, mediating functions such as growth, survival, invasion and angiogenesis in normal cells. Upon binding their appropriate

ligand, a dimerization occurs which induces a conformational change in the receptor that allows phosphorylation of tyrosine residues in the intracellular domain. This then triggers several different intracellular second messenger cascades leading to altered gene expression. Examples of surface RTKs include Kit, epidermal growth factor receptor (EGFR), vascular endothelial growth factor receptor (VEGFR), and platelet-derived growth factor receptor (PDGFR). Dysregulation of these RTKs can lead to uncontrolled cell growth and survival and is one of many underlying causes of some cancers. Examples in veterinary medicine include mutations in the Kit in canine and feline mast cell tumors as well as gastrointestinal stomach tumors in dogs.

Dysregulation of the angiogenic RTKs (VEGF and PDGF) are likely present in a variety of canine and feline cancers including injection site sarcomas (feline), osteosarcoma, anal sac anal gland carcinoma, squamous cell carcinoma (canine and feline), thyroid carcinoma and nasal carcinoma. Currently toceranib phosphate (Palladia; Pfizer Animal Health) is fully licensed and Masitinib (Kinavet, ab-science) is conditionally licensed by the FDA for treatment in canine mast cell tumors.

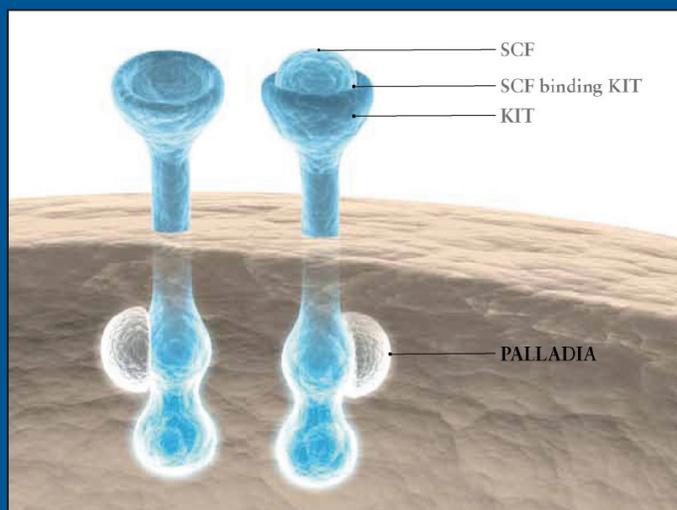


Figure: KIT is a receptor on the surface of mast cell that upon binding its ligand stem cell factor (SCF) will elicit a signaling cascade that leads to growth of mast cells. This signal pathway is mutated in 25% of all mast cell tumors associated with a more aggressive tumor.

What's New in Veterinary Oncology: (continued)

Summary: Clinicians now have a wide variety of novel diagnostics available through commercial laboratories to aid in the diagnosis and prognostication of a variety of canine and feline neoplasia. On the therapy front, two RTKs are

available for use in dogs and several are under investigation. Due to their novel mechanism of action they can be used alongside our current standard therapies consisting of surgery, radiation therapy and chemotherapy.

References:

1. Lana SE, Jackson TL, Burnett RC, et al. Utility of polymerase chain reaction for analysis of antigen receptor rearrangement in staging and predicting prognosis in dogs with lymphoma. *JVIM* 2006;20:329-334.
2. London CA, Malpas PB, Wood-Follis SL, et al. Multi-center, placebo-controlled, double-blind, randomized study of oral toceranib phosphate (SU11654), a receptor tyrosine kinase inhibitor, for the treatment of dogs with recurrent (either local or distant) mast cell tumor following surgical excision. *Clin Cancer Res.* 2009;15:3856-3865.
3. C London, T Mathie, N Stingle, CA Clifford et al. Preliminary evidence for biologic activity of toceranib phosphate (Palladia®) in solid tumours. *Veterinary and Comparative Oncology 2012 In Press.*
4. Hahn KA, Ogilvie G, Rusk T, et al. Masitinib is safe and effective for the treatment of canine mast cell tumors. *J Vet Intern Med.* 2008;22:1301-1309.



NURSES TIP

Angie Itterly, CVT

Etubes- Save a Life!!

Esophageal feeding tubes (Etubes), are indicated in dogs and cats for nutritional support, administration of medications, and for some post surgical cases such as maxillectomies and mandibulectomies. Esophageal feeding tubes are generally well tolerated, have good client compliance, are aesthetically pleasing, and are a minimally invasive procedure. Contraindications include esophageal dysfunction, such as megaesophagus, esophagitis, esophageal stricture and persistent vomiting.

Items needed: 12 or 14 French red rubber catheter, 15 scapel blade, curved hemostats, Sharpie marker, mouth gag, 3 way stopcock, 3-0 Ethilon with cutting needle

Tube prep: Cut across the tube on the distal end where the small hole is. Use a lighter to burn the end so it is not sharp. (Make sure not to melt the hole closed!)

Procedure:

1. Place pet under general anesthesia in right lateral recumbancy
2. Clip and sterile prep the area from the base of the head to in front of the shoulder.
3. Place the distal end of the tip along the ribcage to the area of the heart base. Measure from the tip to the anticipated incision area on the neck and mark a line on the tube.
4. Place a mouth gag and insert the curved hemostat into the esophagus. Position the tip of the hemostat above the jugular vein and below the thick muscle of the neck.

5. Use the scapel blade to dissect through the skin to the tip of the hemostat, and push the tip up through the hole.
6. Open the hemostat and pinch the distal end of the feeding tube within the jaws and lock the handle.
7. Pull the tube through the hole and out the front of the mouth. Attach stopcock and cap on other end so the tube doesn't get pulled through all the way.
8. Place pet in sternal recumbency and use your finger to bend and flip the distal end of the tube back down the esophagus.
9. Using 3-0 Ethilon, place one skin suture. Leave 3-4 inches of extra suture before tying the knot. Loosely tie the suture around the tube to secure it for transport to radiology.
10. Take a lateral chest radiograph to confirm the tube is in the esophagus and is properly placed at the heart base (vomiting can occur if tube is not placed properly). Adjust the tube as necessary and re-mark.
11. Do a purse string skin suture around the tube and pull tight.
12. Use a Chinese finger trap technique up the tube (4-6 throws) and knot tightly. (This is why you leave 3-4 inches of suture in the beginning)
13. Apply NeoPredef powder and place a light wrap around the neck.

Removal:

Snip the sutures, pull tube, and apply light wrap over the hole, which will close on its own.



VCVRC has been serving the Lehigh Valley and surrounding areas since 1996. We are dedicated to providing state-of-the-art veterinary care for your patients.

Specialists at Valley Central Veterinary Referral Center

SURGERY

Carlos Hodges, D.V.M., M.S., P.C.

Practice Limited to Surgery

Salvador Galindo, D.V.M.

Practice Limited to Surgery

NUCLEAR MEDICINE

Ronald Hodges, D.V.M., P.C., D.A.C.V.I.M.

INTERNAL MEDICINE

Ronald Hodges, D.V.M., P.C., D.A.C.V.I.M.

Candace Carter, D.V.M., Ph.D., D.A.C.V.I.M.

ONCOLOGY

Craig A Clifford D.V.M., M.S., D.A.C.V.I.M.

Kate Vickery, V.M.D., M.S., D.A.C.V.I.M.

CARDIOLOGY

Dennis Burkett, V.M.D., Ph.D., D.A.C.V.E.C.C., D.A.C.V.I.M.

Meg Sleeper, V.M.D., D.A.C.V.I.M.

BEHAVIOR

Robin Stephan

Animal Behavior Consultant

ACUPUNCTURE

Diane Gabriel, V.M.D., C.V.A.

Lee Simpson, D.V.M., C.V.A., C.V.C.

OPHTHALMOLOGY

Robert Peiffer, D.V.M., Ph.D., D.A.C.V.O.

Mary Landis, V.M.D., M.A.

Practice limited to Ophthalmology

Continuing Education Schedule

Monthly Case Conferences:

The last Thursday of the Month from 12 PM–1 PM. For your convenience we are continuing to offer monthly case meetings thru web conferencing. For more details please call the office.

Discussions about clinical cases with medicine and surgical implications.

Lunch will be provided, courtesy of Hills, by Dr. Heather Berst.

Until our new web-site is launched, please refer to our Facebook page for updates to our CE schedule.

You may also email Dr. Carlos at Carlos@vcvrh.com with any questions about upcoming lectures.

