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Corneal Collagen Cross-Linking — Another Livs First

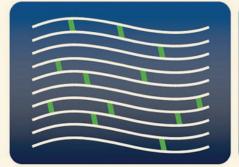
John S. Sapienza, DVM, Diplomate, ACVO

orneal collagen cross-linking (CXL) is a technology whereby the corneal stroma is exposed to the B vitamin riboflavin, which is then photo-activated by exposure to ultraviolet A (UV-A) light. The purpose of the CXL is to create intrafibrillar covalent bonds in the collagen fibers of the corneal stroma to strengthen these bonds. Riboflavin absorbs the UV-A producing reactive oxygen species (ROS), and these free radicals introduce new cross links between the corneal stromal fibers to increase the biomechanical stability of the cornea. CXL was developed to treat corneal ectasia disorders in humans, specifically keratoconus, but additional therapeutic options include infectious and non-infectious keratomalacia ("melting ulcers"). There are several references in the veterinary ophthalmology literature where CXL has greatly improved the healing process of severe corneal melting

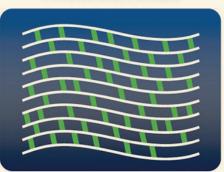
ulcers, and thus surgery was avoided in these cases. CXL has also been successful in the therapy of corneal ulcers associated with bullous keratopathy in dogs. Several great advantages of the CXL procedure over surgical intervention include: much reduced corneal scarring, no risk of anesthesia, lower cost to the client, and often more rapid corneal healing.

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BEFORE CXL : LESS CROSSLINKING = WEAKER CORNEA



AFTER CXL: MORE CROSSLINKING = STRONGER CORNEA



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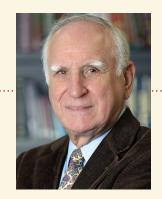




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A Note from the Editor



Glorious days are uplifting and many more are projected for the coming weeks, even months; an invitation to enjoy the summer. Mother Earth is showing us who is in charge however, as volcanic eruptions, flowing lava and fires in Hawaii attest to her power in and on our planet.

Political eruptions, at least from many cable news networks, are rampant and becloud conversation that makes civil discourse almost impossible. A recent essay in Newsday highlighted this fact and decried the inability to discuss viewpoints peacefully rather than incite protests which are becoming increasingly more violent, some even provoked by our duly elected representatives. A NY Times commentary reflected on a need in colleges and universities for speech to be confutative and which must make students uncomfortable, stimulating thought processes with free discussion, not physical shutdown of disparate views.

Students from the area veterinary technician schools are observing the procedures at LIVS and some visiting veterinarians are doing the same. In the ophthalmology department, Dr. Kellam Bayley from New Zealand spent time observing Drs. John Sapienza and Kay Kim.

Dr. Meghan Umstead has extended hours to offer services to our clients and referring veterinarians and is available to consult in cases that need direction and appropriate allergic management. The Internal Medicine Department under Dr. Joshua Tumulty's direction, has expanded appointment availability for elective and emergency internal medicine consultations and ultrasound evaluations Monday through Saturdays. Dr. Curtis Dewey, associate professor and section head of Neurology/Neurosurgery at the College of Veterinary Medicine at Cornell is at LIVS regularly for consultation as is our animal behaviorist, Dr. Sabrina Poggiagliolmi. Appointments can be made at 516-501-1700. Feel free to contact any of the aforementioned staff members about how they may be of service.

As before we welcome all comments, please submit them to lmarino@livs.org

Leonard J. Marino, MD, FAAP, LVT

Corneal Collagen Cross-Linking— Another Livs First

➤ Continued from Front Cover

There exist several protocols as well as CXL units on the market. In summary, the patient is mildly sedated or just topical proparacaine anesthesia is applied in high risk anesthesia patients, and then topical riboflavin, which is specifically formulated for the cornea, is applied for 15-20 minutes. The cornea is then evaluated by slit-lamp biomicroscopy to assure proper absorption of the riboflavin into the corneal stroma and into the anterior chamber. The cornea is then exposed to a special UV-A light in order to activate photodynamically the riboflavin within the corneal stroma. The unit that we use allows irradiation of the cornea at 45 mW/cm2 for only 2 minutes of treatment time.

malacia and corneal abscessation with remarkable results. The healing process is accelerated, and the post-CXL corneal scarring is incredibly less as compared to a corneal grafting procedure. The procedure was well tolerated by all patients with very light sedation (typically only tobugesic via injection) and topical anesthesia drops.

Contraindications: CXL can lead to herpesvirus exacerbation in humans. In a study by Famose in the Veterinary Ophthalmology journal, CXL did not cause any reactivation in two cats positive for feline herpesvirus. CXL should not be used in cats with active herpesvirus infection. In addition, CXL is not advised in corneas thinner than 400 µm, as this may

lead to endothelial damage or damage to the intraocular structures.

The CXL is another resource in our armamentarium in the battle against corneal diseases in dogs. The process is not 100% successful for all keratomalacia cases, as the enzymatic degradation of the cornea may weaken the stromal thickness and require corneal surgery in a select few cases. So far, our overall impression is quite favorable with CXL in dogs, and we are the only facility in our metropolitan area to offer this novel therapy for melting corneal ulcers, keratoconus and ulcers associated with bullous keratopathy.

Any questions or concerns, please do not hesitate to call us. $\hfill \square$

Cornea Keratomalacia

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Figure 1: Cornea CXL preop

Figure 2: Cornea CXL first week post op

Figure 3: Comea CXL three weeks post op









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Managing Acute Pain — Myths and Tips for A Rational Approach to Pain Management

Meredith von Roedern, DVM, Diplomate, ACVECC

he two most damaging and outdated myths regarding pain management that I have come across are:

Myth 1: It is better for the patient to undertreat pain so that they will not "overdo it" after a surgery or injury

Myth 2: Better to have a painful patient that is alive than a patient dead from the side effects of pain medications

These myths are both based on a significant false premise that pain does not have adverse consequences that can cause morbidity and mortality and/or the side effects of pain are less dangerous than the side effects associated with treating pain.

Reality: There are many consequences of untreated pain. Pain is not benign and many of these consequences can potentially affect a patient's outcome.

- Pain causes immobility, which decreases the movement of venous blood and lymph. Venous stasis contributes to hypercoagulability and increased risk of clots including PTE. Decreased lymph movement can promote the accumulation of peripheral edema which can lead to delayed wound healing. Immobility will also exacerbate OA and lead to increased pain.
- Pain can also negatively impact the respiratory system. Pain can cause hypoventilation; it frequently causes animals to take rapid shallow breaths which can lead to atelectasis and decreased pulmonary function. Patients may be less willing to cough, as this can exacerbate pain, so they tend to retain pulmonary secretions with places them at increased risk of pneumonia.
- Pain can be a potent stimulator of the autonomic nervous system, specifically increasing sympathetic tone. This causes peripheral vasoconstriction, which will decrease blood flow in the skin and to incisions/wounds/injuries which will delay wound healing.
- Increase in sympathetic tone can also cause systemic hypertension and tachycardia, which increases the workload on the heart leading to increased myocardial oxygen demand and consumption. This can lead to arrhythmias and may predispose a patient to fluid overload.
- Activation of the sympathetic nervous system also causes decreased blood flow to the GI tract and suppresses parasympathetic function which leads to ileus

- and inappetence. Pain can even directly stimulate nausea in the chemoreceptor trigger zone and vomiting center within the brain resulting in emesis which can result in aspiration pneumonia.
- Additionally, acute pain can result in wind up pain, which can result in chronic maladaptive pain and hyperalgesia. These types of pain can persist indefinitely and can have a very significant impact on quality of life in people and likely occurs in some animals as well.
- Unrelieved pain can cause immunosuppression via the upregulation of cortisol and other mediators. Immune suppression can increase the risk of wound infection, catheter associated infections, pneumonia and sepsis.
- Pain can keep animals from sleeping, which can lead to delirium and delayed healing.
- Pain can lead to aggression, which makes them more difficult to handle and evaluate, and not to be forgotten, pain causes significant suffering, which is something that veterinarians have pledged themselves to alleviate as part of the veteri-

There are many consequences of untreated pain. Pain is not benign and many of these consequences can potentially affect a patient's outcome.

Given all of the negative consequences of pain, it is no longer acceptable to inadequately treat pain to avoid the side effects of pain medications. The more we learn about multimodal pain therapy, the better we can treat patient pain, allowing us to avoid the negative consequences of pain, while minimizing the side effects of the pain medications and improving patient overall wellbeing.

There may be situations where pain meds need to be temporarily delayed, however, I would argue that even these situations are rare. Even animals that are relatively unstable may benefit from pain medications because



they may not be able to tolerate the increased myocardial and tissue oxygen demands caused by additional sympathetic stimulation. Pain medications do occasionally need to be delayed for a short time to allow adequate assessment of a patient's injuries and/or neurologic status, however, these assessments should be undertaken as quickly as possible and then pain medications should be admin-

There are many ways to ensure that an animal does not cause itself further injury after a procedure or injury that do not necessitate inadequate control of pain. These animals can be strictly confined, a bandage or splint can be placed and overexcitement and agitation can be controlled pharmacologically as needed.

Tips for a rational approach to pain management

Tip 1: Individual approach

One size does not fit all when it comes to managing pain. Pain medications do have side effects some of which can be detrimental to the patient under certain circumstances. The most appropriate pain management plan is the one that is individually tailored to the patient factoring in age, comorbid conditions, nature and severity of injuries and pain, etc.

Tip 2: Pre-emptive therapy

Pain is easier to control with less medication when treated early and before it is severe, or ideally before it starts. Pre-emptive analgesia is not possible in animals that present for trauma, but can be incredibly beneficial in surgical patients where the pre-medication prior to surgery should include a strong analgesic.

Tip 3: Multimodal therapy (pharmacological and non-pharmacological)

Combining multiple analgesics with different

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mechanisms of action and that act at different sites in the pain pathway allows for lower doses of individual drugs, which may help limit the adverse side effects of each individual medication while still adequately managing pain (see figure 1). There are many medications as well as non-pharmacological options that can be used together to treat acute pain including:

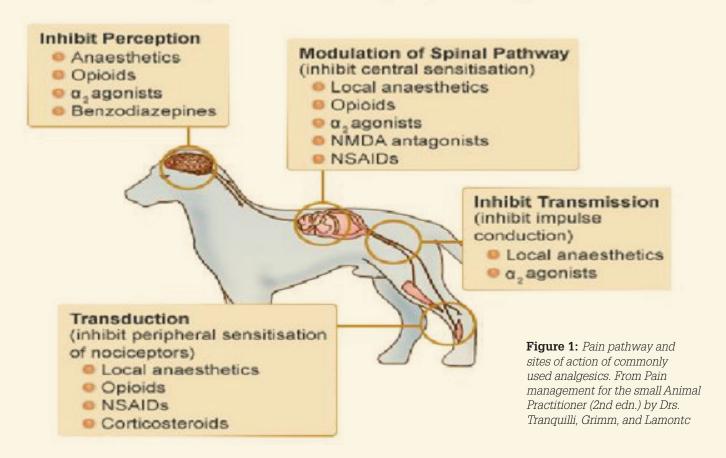
Opioids: Opioids are a mainstay for treating acute, moderate to severe pain in people and in animals. They are some of the strongest analgesics we have. Moderate to severe acute pain typically requires opioid therapy in addition to adjunctive analgesics to achieve adequate analgesia. There are many pure mu injectable opioids available, and in general they have similar safety and efficacy profiles. Efficacy of these drugs depends on using them at adequate doses on an appropriate schedule which will vary from drug to drug. Buprenorphine is a partial mu opioid; it binds the mu opioid receptors but causes only a partial response with a "ceiling effect" where escalating doses do not result in increased analgesic efficacy beyond a certain dose. While buprenorphine is nice because there also is a "ceiling effect" on side effects, it does have some drawbacks that should be considered before use. The biggest concern for buprenorphine is that it binds the mu receptors very tightly, which prevents the binding of other opioid pain medications and also prevents binding of naloxone. The consequences of this are: 1. If the buprenorphine is not effective enough to control pain, the administration of other pure mu opioids to achieve analgesia is ineffective which may make adequate analgesia difficult to achieve until the buprenorphine wears off. 2. Naloxone will not reverse buprenorphine actions if there are adverse effects or if the patient develops cardiovascular collapse and needs resuscitation, which is a safety concern.

 NSAIDs: NSAIDS are very good analgesics particularly for conditions associated with inflammation (including postsurgical inflammation). NSAIDS should be considered in the pain management protocol unless there are specific contraindications. NSAIDs should be avoided or used with caution in animals with preexisting renal or hepatic disease, concurrent renal toxic medications (diuretics, ace inhibitors, aminoglycosides etc.), hypotension, dehydration and active GI disease. Robenicoxib (Onsior®) can be considered in cats without contraindications for NSAID use.

- Ketamine: Ketamine antagonizes NMDA receptors which are involved in the development of wind up pain/central sensitization. Ketamine is typically administered as a CRI after an initial loading dose
- Local/regional anesthesia: When successfully applied, local nerve blocks or epidurals can completely block the transduction or transmission of pain signals into the central nervous system. This

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Pharmacological intervention of pain processing



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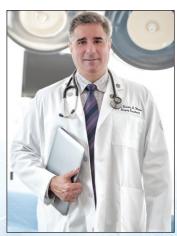
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Managing Acute Pain — Myths and Tips for A Rational Approach to Pain Management

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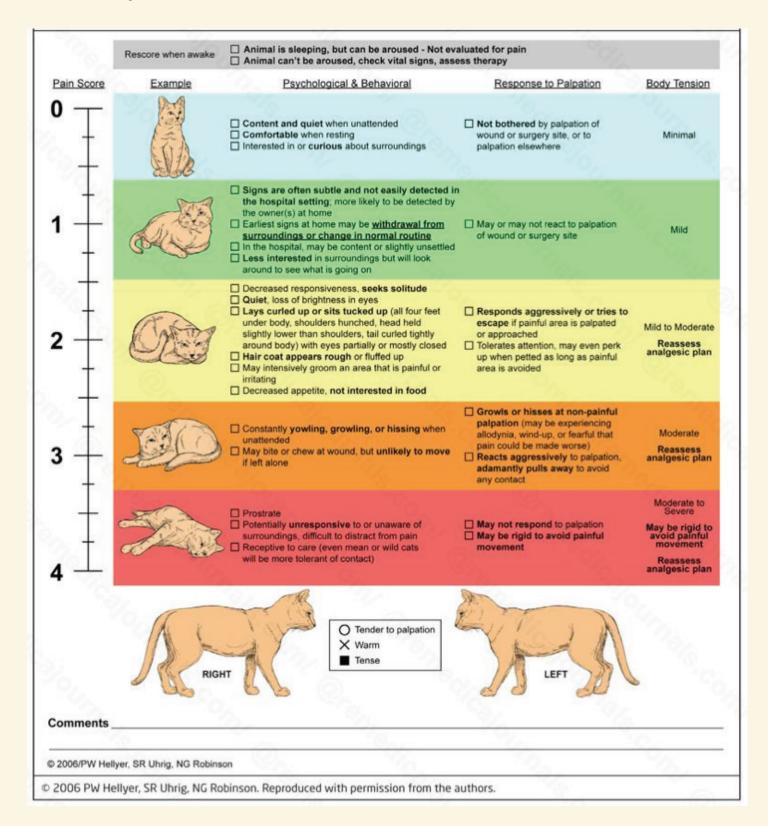


Figure 2: CSUAcute pain scale for cats

Managing Acute Pain — Myths and Tips for A Rational Approach to Pain Management

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can be very helpful in minimizing the drugs needed to maintain anesthesia and improving comfort in the immediate post-operative period. The biggest limitation to local anesthetics is that they wear off relatively rapidly (lidocaine lasts 1-2 hours, bupivacaine lasts 3-6 hours typically). A new product called Nocita® is a liposomal encapsulated bupivacaine whose duration of action is up to 72 hours. This product is currently approved for use in veterinary cruciate ligament repair, but additional uses are likely, and this new medication may have a transformative effect on multimodal pain therapy for veterinary patients in the future due to its extended duration

Non-pharmacologic therapies: There are many non-pharmacologic pain management techniques that can be added to pharmacologic management to treat acute pain including cryotherapy, laser therapy, acupuncture, therapeutic massage and physical therapy. Tip 4: Pain scoring

Pain assessment in animals is subjective and can be very challenging. The best approach to pain assessment is to use a validated veterinary pain scoring system of which there are several (Glasgow Composite Measure Pain Scale, Colorado State Canine/Feline Acute Pain Scale etc.); see figure 2. These composite scales incorporate interactive and behavioral components to assess pain in canine and feline patients. These scales help identify more subtle signs of pain (withdrawn behavior, hunched body posture, decreased interactiveness etc.) to avoid undertreating pain in animals and they allow for a more standardized and repeatable approach to assessing pain between evaluators and over time in any given patient. Pain scoring should be assessed immediately and then re-evaluated frequently in animals currently in or at risk for pain. They should be assessed before and after analgesic therapy to ensure adequate control of pain with their individualized pain management protocols. Pain scales may seem foreign at first, but become quick and easy over time as staff become familiar with their use.



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