LIVS In Plain View

LONG ISLAND VETERINARY SPECIALISTS

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Inside This Issue

Why Is My Dog Sleeping So Much?!?!?!

Ann Bilderback, DVM, DACVIM (Neurology)

Naturally occurring sleep disorders are uncommon in dogs and cats and some can be very challenging to diagnose. For most veterinarians, the goal is not to diagnose a sleep disorder, but rather to different it from the more common disorders that we see such as seizures, myasthenia gravis, syncope, etc. Something to keep in mind if your patient is not responding to the typical treatment for the more common disorders that we see. The focus of this article will be on narcolepsy which is the most well known and studied sleep disorder, but others have been reported as well.

Unlike people, dogs typically sleep 10 or more hours per day while cats can sleep 12-16 hours per day (if only we were so lucky!). Normal sleep is comprised of three phases that humans and animals cycle through:

- **Awake** – when the patient is awake and alert
- **Slow-wave sleep** (a.k.a. non-REM sleep) – "light" sleep
- **Rapid eye movement (REM) sleep** – "deep" sleep

The focus of this article will be on narcolepsy which is the most well known and studied sleep disorder.

During slow-wave sleep, the animal clinically appears asleep. During REM sleep, muscle tone is absent except for rhythmic eye movements, occasional twitching of the face and limb muscles, and mild vocalization may be present – all of which we anthropomorphically associate as "dreaming" in dogs and cats. During sleep, humans and animals cycle through the three phases constantly with approximately 3 hours of sleep spent in periods of REM sleep.

Narcolepsy is a syndrome characterized by abnormalities in the sleep/wake cycle. This can include excessive sleepiness when awake and periods of cataplexy. Cataplexy is a sudden involuntary episode of muscle weakness affecting most of the striated muscles of the body. The sudden involuntary loss of muscle tone is thought to be pathologically equivalent to the lack of muscle tone that is present during REM sleep. The cardiac muscles and mus-

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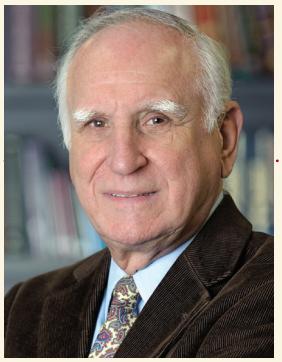
A Note from the Editor



In July, our chief of staff, Dr. Dominic Marino travelled to Guangzhou, Shanghai and Beijing, China to lecture to Veterinarians from China, Taiwan, Thailand and South Africa. Many Orthopedic topics were covered over the 2 weeks trip including Gait Analysis, Lameness Localization, Orthopedic Imaging, and Total Hip Replacement Surgery. Many hospitals were visited and the exchange of information and experiences was invaluable to all who attended. Drs. Liu and Zhang were wonderful hosts and made the cultural experience quite amazing.

On the return trip from China, there was a stop in Dubai, where the average temperature in late July is 98 degrees F. Nonetheless that emirate is home to the tallest building in the world and the largest shopping mall as well. Built using oil money, oil now accounts for less than 5% of its income as tourism, money and investment transactions, shipping and trade bring in the bulk of income. Most of the inhabitants are from India and only 20% or so are actual Arabs originating from the territory facing the Persian Gulf. Police cars may be Ferraris, even Lamborghinis in some instances and like in Iran, over half of the university students are female. At one point, the natives supported themselves by diving for pearls but that ended when the Japanese found a way to produce cultured pearls. The visionary emir developed a tax free port and built another before the first was even completed, then bought dozens of airliners just after 9/11 when people were hesitant to fly and prices were low. Emirates Airlines is well known for its luxurious flying experience even if its fees are hardly in the economy sphere.

The warmest months are here and on really hot days, asphalt can reach a sizzling 135 degrees — more than hot enough to cause burns, permanent damage and scarring after just a minute of contact. Hot sidewalks, pavement and parking lots can not only burn paws, they also reflect heat onto dogs' bodies, increasing their risk of heatstroke. It's prudent to walk early in the morning or late at night when it's cooler and be careful with muzzles that restrict breathing.

A common inhabitant of canine and feline saliva, Capnocytophaga canimorsus, is rarely a cause of severe problems but on occasion causes a life threatening illness especially in immunologically compromised individuals, those who are asplenic and alcoholics. A recent survivor lost both hands and needed below knee amputations because of diminished blood flow to the extremities. He was not bitten but just licked; neverthetless sepsis set in! Love pooches but allowing face licking; not wise.

Schools are beginning to open and restrictions on speech are ominously ever present. Professor of Linguistics John McWhorter at Columbia said campuses are supposed to be realms of bold inquiry and fearless debate. Law Prof Stephen Carter at Yale said we must not squelch upsetting words with odious behavior. As I see six of my grandkids heading off to college I think of the remark made to a local priest by Voltaire: "Monsieur l'Abbé, je déteste ce que vous écrivez, mais je donnerais ma vie pour que vous puissiez continuer à écrire",

(My dear Father, I detest what you write, but I would give my life so that you may continue to write). Monsieur l'Abbe' is a deferential French term for priests, though they may not all be Abbots.

It seems that now, some protesters are saying "I detest what you say and you will give your life if you continue to say it." Francis of Assisi, Gandhi and ML King protested non-violently yet successfully.

We have lost Sen. John McCain to glioblastoma, his public words fit the description of civil discourse.

We are pleased to be able to continue to 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.

Leonard J. Marino, MD, FAAP, LVT

Why Is My Dog Sleeping So Much?!?!?!

➤ *Continued from Front Cover*

cles of respiration are not affected and continue to function normally.

Pathophysiology

The sleep cycle is directed by sleep centers in the brainstem which affects the reticular activating system (RAS). One function of the RAS is to help to alert, or awaken, other parts of the brain, such as the cerebral cortex. It is responsible for regulating arousal and sleep-wake transitions which helps to keep us alert and conscious.

Specific neuropeptides, known as hypocretins1 and 2 produced in the hypothalamus, have been found to be critical in regulating the sleep/wake cycle. Hypocretin-producing neurons project to areas in the brain and spinal cord, including areas of the RAS. These hypocretin-producing neurons control and coordinate normal sleep, promote a wakeful state, and are involved in the regulation of motor function (e.g. locomotion, muscle tone). Hypocretins typically have an excitatory effect on the RAS and are responsible for inhibiting REM sleep.

Narcolepsy is due to a malfunction of the hypocretin system, either due to a deficiency of the hypocretin neuropeptide itself or due to a mutation of the hypocretin receptor. Clinical signs of narcolepsy reflect the lack of hypocretin-mediated inhibition of REM sleep and lack of hypocretin's excitatory influence on the RAS which normally functions to promote an alert/awake state.

Forms of Narcolepsy

Narcolepsy is caused by either

1. The loss of production of hypocretin neuropeptides due to absence or destruction of hypocretin-producing cells in the hypothalamus
2. The absence of hypocretin receptors on target cells
3. As a result acquired CNS disease (i.e. secondary to pituitary tumor, other intracranial disease) – this is a very rare cause of narcolepsy and has only been reported sporadically

The most common form of narcolepsy occurs sporadically and is associated with deficiency of the hypocretin neuropeptides. Age of onset is variable and can start as early as 6 months of age but typically occurs in adult dogs (mean age of onset 2.4 years). The sporadic form can occur in dogs of any breed.

A familial form of narcolepsy is caused by mutations in the hypocretin-receptor-2 gene and has been documented in Doberman Pinschers, Labrador Retrievers and Dachshunds as an autosomal recessive mutation. Onset of clinical signs may occur as early as 4 weeks of age, but in mild cases clinical signs may not be obvious until 6 months of age.

Clinical Signs

Cataplexy (sudden involuntary loss of muscle tone) is usually the most prominent clinical sign. Animals may be affected profoundly and collapse suddenly to the floor without any warning, remaining motionless. There is partial to complete hypotonic or atonic ("limp") paralysis that may involve all striated muscles or be restricted to certain limbs or the head and trunk. Although affected animals may appear unconscious, in actuality, they usually remain conscious during the episodes and often will visually "track" moving objects with their eyes. However, if the episode lasts more than several minutes, the animal may experience sudden onset REM sleep with rapid eye movements and twitching of the facial and limb muscles.

Milder cataplectic episodes may manifest as transient "weakness" causing an ataxic appearing gait. The limbs may appear to "give out" and head and neck may appear weak with a sense that the animal is struggling to resist the "sleepiness." Some may continue on to complete collapse.

Cataplectic episodes are usually elicited by excitement, such as food, water, or play, but can also occur spontaneously. The duration varies from a few seconds to 30 minutes or more. These episodes can occur suddenly and end just as quickly. Sensory stimulation (e.g. loud noise) or physical stimulation (e.g. gentle shaking) will often interrupt the cataplectic episode.

Excessive sleepiness is recognized in many affected dogs. Several manifestations include prolonged periods of normal sleep, difficulty arousing the patient during sleep, appearing drowsy throughout the day along with inability to remain awake for normal periods of time, and sudden onset of REM sleep from an active state (i.e. sleep attack).

Diagnosis

Diagnosing narcolepsy is based on cataplectic attacks triggered by excitement – such as food or playing. Other disorders that can be episodic should be excluded, such as seizures, syncope, myasthenia gravis, etc. If an episode cannot be elicited at time of evaluation, the owner should obtain a videotape of the episodes at home. Direct (or indirect via video) observation of the episode is essential in determining the nature of the episodes and avoiding costly misdiagnoses or frustrations should inappropriate therapy be initiated.

A cataplectic episode may be elicited by testing the patient with excitement. For those that love to eat or for those that love to play, an episode may be elicited by feeding the patient or playing with the patient. A food test is most often used in the clinical setting. However, in some patients the test may be unreliable in the clinical setting due to the strange or stressful environment. In that situation, it may be more useful to have the owner videotape the test being performed at home.

The excitement test above has been effective for the author in diagnosing patients with narcolepsy/cataplexy. However, in mildly affected animals that do not respond to excitement testing, a cataplectic attack may be diagnosed with IV physostigmine salicylate (cholinesterase inhibitor) which increases the chances of cataplexy occurring within 15 minutes. Furthermore, in patients with sporadic narcolepsy, measuring CSF concentration of hypocretin-1 is possible with low levels confirming the diagnosis of narcolepsy. However, normal levels of CSF hypocretin does not exclude the diagnosis of narcolepsy as dogs with a mutation in the hypocretin-receptor will have normal levels of hypocretin (i.e. familial narcolepsy).

Treatment

The most prominent clinical sign in narcoleptic dogs is cataplexy and treatment of narcolepsy is aimed primarily at reducing the frequency and severity/duration of the cataplectic attacks. In mildly affected dogs, avoiding the

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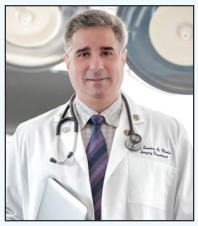

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inciting cause may be the best treatment. Avoiding or limiting the excitement or play behaviors that stimulate the cataplectic episodes should be avoided when possible. In dogs that live in multi-dog households, feeding separately or at different times from the other dogs in the household may reduce the number of cataplectic episodes.

In severely affected dogs, the above changes in behavior along with medications should be considered. Medications that activate the adrenergic system may lead to reducing the cataplectic episodes. Cataplexy is usually treated with antidepressants such as

- **Tricyclic antidepressants** (TCAs), such as imipramine, protriptyline, and amitriptyline, act via blocking norepinephrine reuptake in the CNS.
- **Selective serotonin reuptake inhibitors** (SSRIs) may also be effective, such as fluoxetine.

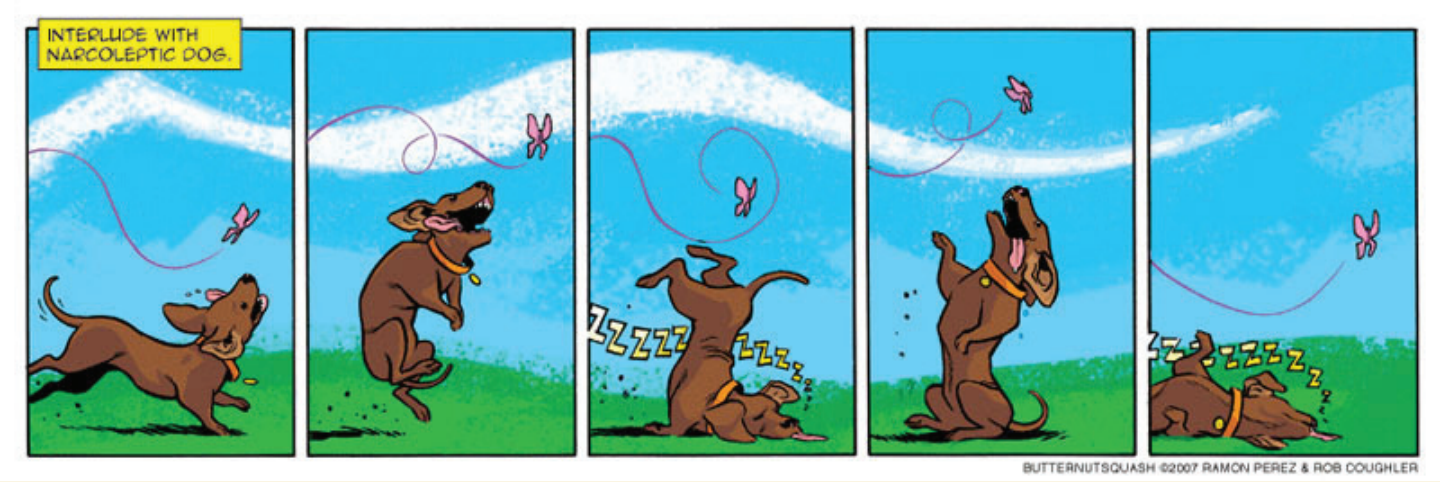
Imipramine is the author's first choice as imipramine is not only a TCA but also blocks serotonin reuptake.

Excessive sleepiness may occur with narcolepsy, but this component has minor impact on narcoleptic dogs and their owners and is usually not treated. However, in those patients where it is severe and impacts quality of life, excessive sleepiness can be treated with stimulants such as

- **Alpha-2 antagonist:** yohimbine
- **CNS-like stimulants:** modafinil
- **Other CNS stimulants:** methylphenidate, dextroamphetamine, pemoline, selegiline

Prognosis

Canine narcolepsy is not a life-threatening or progressive disease, but the clinical signs persist throughout life and some dogs may even improve without treatment. Although there is no cure for narcolepsy, medication is often effective at minimizing and controlling clinical signs. With client education, avoidance of the inciting factors where possible, medications when needed, and adjusting the home environment (unbreakable food bowls, elevating water bowls to prevent drowning/aspiration during cataplectic attacks, etc.), narcoleptic dogs may have a good quality of life. ❑



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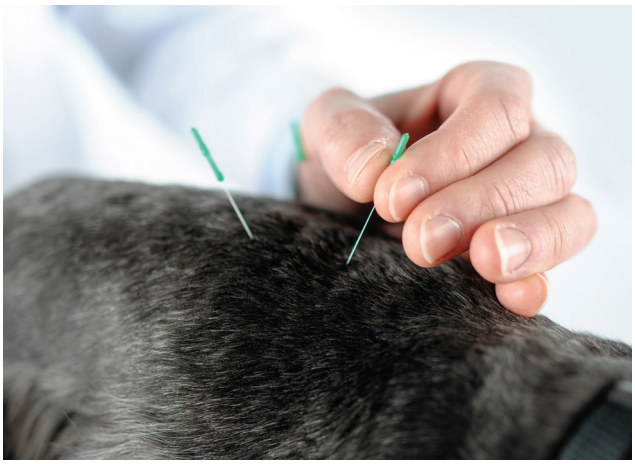

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John S. Sapienza, DVM, Diplomate, ACVO

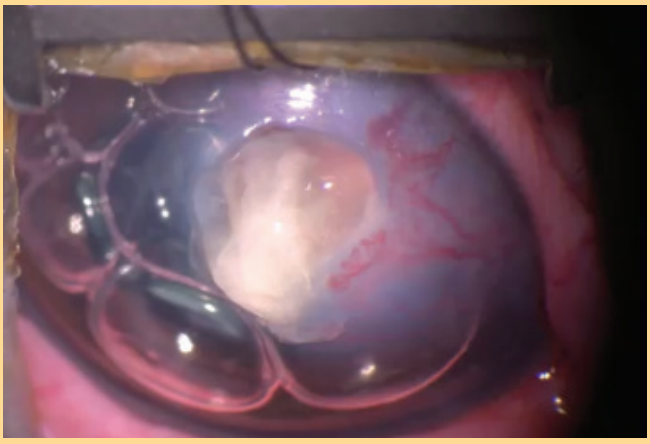
When presented with a deep corneal ulcer in our patients, several surgical options exist. The choice of one surgery over another depends on several factors: location of the defect (central vs peripheral), depth of the lesion (deep vs superficial), presence or absence of infection, and the desire to minimize any corneal scarring. Appropriate surgical techniques include a donor corneal graft, conjunctival grafting, amnion membrane tissue, various porcine grafts (Biosis, A-cell) and recently an acellular porcine cornea graft.

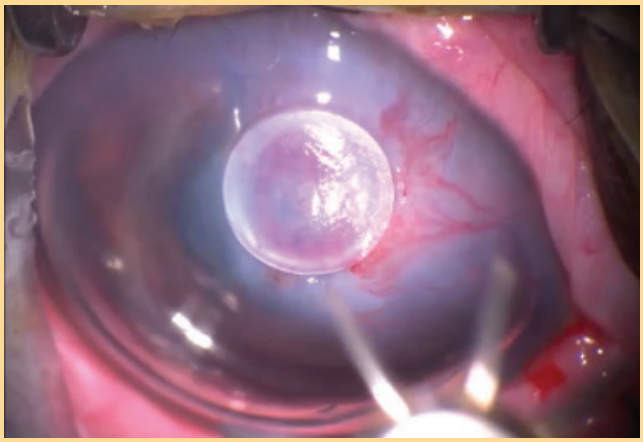
We have been selected as a premier ophthalmic referral center to participate in the use of this acellular porcine graft in dogs with complicated corneal ulcers. An ideal scaffold for a tissue-engineered cornea should have good biocompatibility, high optical clarity, toughness to withstand surgical procedures and non-immunogenicitic properties. Porcine collagen is well tolerated after heterogeneous implantation, and shares similar anatomic characteristics with both THE animal and human cornea. Previous research has showed that an acellular porcine cornea matrix could preserve the key features of the cornea, including the intact basement membrane, and support the growth of corneal epithelial cells and fibroblasts or human embryonic stem cells-limbal stem cells.

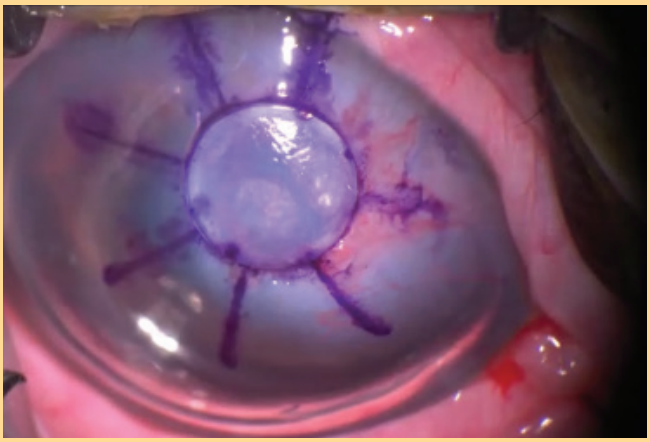
Under sterile surgical conditions, the corneal defect is prepared for receipt of the porcine graft. Any infected tissue is removed by sharp dissection and debridement. The depth of the corneal defect is assessed by pachymetry, which employs a unit that allows us to precisely measure the corneal depth in vivo. Once the corneal ulcer is ready for the donor acellular cornea, precise microsurgical technique is required to properly suture the graft into the defect. Using high power magnification of the operating microscope, the graft is typically sutured in place with 9-0 or 10-0 suture material.

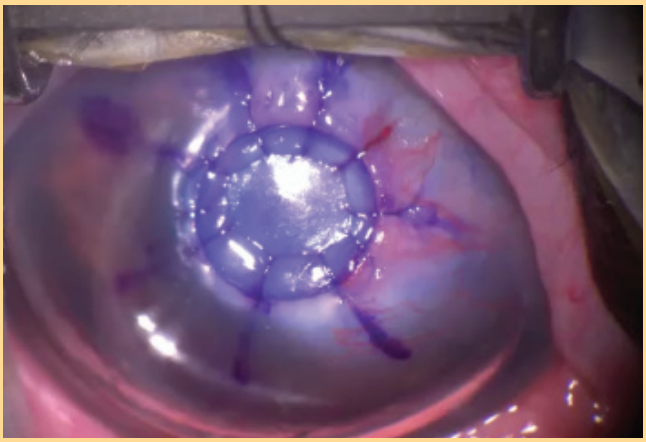
The Acceptance of this porcine corneal graft is widely known to be due to the acellular nature of the graft. The initial findings of this graft show a moderate vascular response after an initial bullous condition. Topical antibiotics, cycloplegia and oral anti-inflammatory medications are prescribed. The long-term clarity of this porcine graft is excellent, and especially useful for central corneal lesions where transparency is imperative.

We are very excited to participate in this ground-breaking technology and offer this as another option in our surgical repertoire. If you have any questions or concerns, please do not hesitate to contact us. ❑









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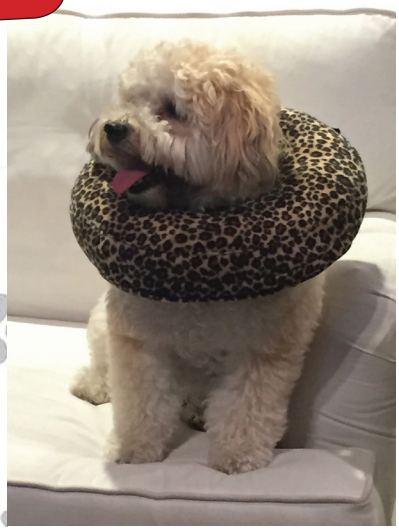

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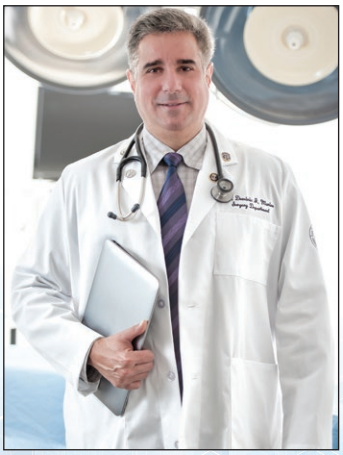

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