AMERICAN ASSOCIATION OF FELINE PRACTITIONERS

2023 Spring into Feline Medicine

THREE-DAY ***VIRTUAL LIVE CE EVENT***

Sunday, April 30th | Wednesday, May 10th | Saturday, May 20th

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THREE-DAY **VIRTUAL LIVE CE EVENT**

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ALL TIMES ARE EASTERN TIME ZONE

Sunday, April 30, 2023

TIME	SESSION TITLE	SPEAKER	SPONSOR/PARTNER
12:00 - 1:00 pm	The Cat is Losing Hair: It's Not Allergies & it's Not Dermatophytes, Now What?	Dr. Catherine Outerbridge	wedgewood PHARMACY
1:15 - 2:30 pm	Feline Regional Dermatoses: Skin Diseases that Target the Dorsal Muzzle, Footpads, or Sometimes Both	Dr. Catherine Outerbridge	
2:45 - 3:45 pm	The Do's and Don't's of Trauma	Dr. Steven Berkowitz	
4:00 - 5:00 pm	Feline Respiratory Emergencies: "Stat: Why is My Cat Panting?!"	Dr. Steven Berkowitz	

Wednesday, May 10, 2023

TIME	SESSION TITLE	SPEAKER	SPONSOR/PARTNER
2:00 - 3:00 pm	A Bright Future for Painful Cats: New, Improved, & Emerging Options for Multimodal Management of Feline Osteoarthritis	Dr. Erin Dresner	
3:15 - 4:15 pm	Feline Neurology: Pearls for Your Practice	Dr. Joane Parent	
4:30 - 5:30 pm	Improving Interpretation of Pulmonary Patterns	Dr. Lorrie Gaschen	
5:45 - 7:00 pm	FIP Updates: Optimizing Treatment Now & Into the Future	Dr. Sally Jayne Coggins	

Saturday, May 20, 2023

TIME	SESSION TITLE	SPEAKER	SPONSOR/PARTNER
12:00 - 1:00 pm	Management of Oral & Dental Pain	Dr. Heidi Lobprise	IVAPM
1:15 - 2:30 pm	Feline Stomatitis	Dr. Heidi Lobprise	
2:45 - 3:45 pm	Anterior Uveitis: Don't Miss The Big Stuff	Dr. Jessica Meekins	Dechra
4:00 - 5:00 pm	The Crystalluria Dilemma: When Should I Care About Crystals?	Dr. Julie Byron	ROYAL CANIN

American Association of Feline Practitioners
2023 Spring into Feline Medicine ● April 30, May 10 & May 20

The Cat is Losing Hair: It's Not Allergies and It's Not Dermatophytes, Now What?

Catherine Outerbridge, DVM, MVSc, DACVIM (SAIM), DACVD

Introduction

As the skin is readily visible, any changes in coat quality or the development of hair loss is often of concern to feline pet parents. Investigating what is causing alopecia means determining the reason for loss or absence of hair and can present challenges as there are many different etiologies and it is even possible to have more than one etiology in the same cat.

It can be more helpful to think of broad mechanisms that could result in hair loss.

1. Alopecia often occurs because of self-trauma in pruritic cats. Pruritic behaviors to relieve itch can remove the hair at the skin surface. If pruritic behaviors are identified and the hair loss is clinically compatible with self-traumatic alopecia (broken hairs) then the cat needs to be evaluated for causes of pruritus, in particular causes of feline allergic dermatitis or ectoparasites. Psychogenic self-traumatic alopecia in the cat is in fact quite rare.
2. Infectious folliculitis can have 3 main causes in cats dermatophytosis, bacterial folliculitis, and *Demodex cati* (*Demodex gatoi* is a non-follicular mite and a cause of self-traumatic alopecia). Dermatophyte infections weaken the hair shaft causing it to break; and the inflamed follicle from any infectious cause may not initiate anagen to regrow its hair shaft.
3. Non-infectious causes of primary hair follicular pathology have numerous etiologies including endocrinopathies, paraneoplastic causes, and immune-mediated diseases all disrupt the structure or follicle cycling of the hair follicles.
4. Alopecia can result from pathology of the hair shaft itself (think of hairless breeds that often produce a defective hair keratin).

For the purpose of this lecture, we will focus predominantly on non-infectious, non-self-traumatic causes of alopecia in cats.

Hair Follicle Anatomy & Physiology

The hair follicles are divided into different portions. These regions are referred to in pathology reports to indicate what area of the follicle is involved and how deep the follicular lesions are. Certain diseases affect certain portions of the hair follicle

- Infundibulum: the superficial portion, which opens into the orifice of the follicle. The epithelium of the infundibulum is equivalent to the epidermis
- Isthmus: the middle portion includes the bulge, the location of the follicular stem cells.
- Supra-bulbar area and bulb: are deep portions of the hair follicle

Hair growth is cyclic, and guided by numerous growth factors and enzymes, which affect various stages of the cycle. The following are the phases of the hair cycle:

- Anagen (growth phase**):** The *duration* of the anagen phase dictates the length of the hair shaft so short coated animals have a shorter anagen phase
- Catagen (transitional phase): typically short phase, the follicle involutes and transitions to rest.
- Telogen (resting phase**)**: the longest phase in the cycle, the hair shaft should stay in the hair follicle ("haired telogen") until the new anagen hair growing from underneath "pushes" this out. The hair follicles still contain a hair shaft, which is anchored to the follicular epithelium only by a keratin plug. This anchorage is not as firm as the anchorage to a hair bulb and papilla. Hence, telogen hair shafts can be epilated more easily than anagen hairs.
- Exogen stage: the old hair is pushed out when the new anagen is starting
- Kenogen stage: The hair follicle is involuted and has no longer a hair shaft present. This is also referred to as hairless telogen

Dermatologic History & Derm Data Base

It is critical whenever assessing alopecia in a cat to obtain a thorough dermatologic history and obtain answers to questions about overall systemic health including weight loss, appetite and presence of polyuria or polydipsia, or other systemic clinical signs.

When the presenting complaint is hair loss it is important to determine if there is any evidence for self-trauma either observed supportive behaviors, other lesions compatible with self-trauma (excoriations, linear lesions) and evaluating hair shaft integrity on a trichogram.

Age of onset is important, as congenital alopecia is often present at birth or shortly thereafter. Some diseases are more likely to develop in older cats. Determining what past therapies have been tried and what if any clinical response has occurred is also important historical information. Cats that improve when administered corticosteroids should be closely assessed for possible underlying pruritic skin diseases. Any past corticosteroid, administration should be critically evaluated to ensure that hypercortisolemia has not influenced hair follicle function.

A dermatologic database should include a trichogram to assess hair shaft integrity, a Wood's Lamp to screen for possible dermatophytosis, surface cytology for evidence of secondary infections, and samples to evaluate for potential ectoparasites. As the most common causes of alopecia in the cat are 1) self-trauma to relieve pruritus, due to possible allergic dermatitis, or ectoparasites and. 2) dermatophytosis further diagnostic tests to consider are fungal PCR or culture to rule out possible dermatophytes and evaluation for allergic dermatitis. For some of the disease to be discussed systemic evaluation with CBC or serum biochemistry or imaging may be warranted and potentially skin biopsies.

Self-traumatic/self-induced alopecia

Over grooming in cats for behavioral and psychogenic causes is in fact uncommon and is likely over diagnosed. The majority of cats with self-induced alopecia are in fact pruritic cats; this was confirmed in a study evaluating cats for psychogenic alopecia, where in 90% of the cats an underlying pruritic disease was diagnosed[1]. It is critical to effectively rule out underlying causes of pruritic disease before ever considering A diagnosis of psychogenic alopecia. Flea allergy, feline atopic skin syndrome +/- cutaneous adverse food reaction, infections (dermatophytes, *Malassezia,* bacterial) and ectoparasites should all be evaluated for. Clinically self-traumatic alopecia can have concurrent inflammation (erythema, scale, hemorrhagic crusts); the broken hairs are palpably more coarse and there may be visible variation in the length of hairs. If over grooming behavior is documented and/or on a trichogram broken hair shafts are evident than the cat should be evaluated for causes of pruritus.

Psychogenic alopecia can only be diagnosed when all other organic causes of disease have been ruled out. Commonly affected areas include medial forelegs, caudal abdomen, inguinal region, tail and/or dorsal lumbar areas (often lesions are bilaterally symmetric). Psychogenic alopecia reportedly occurs more commonly in strictly indoor cats. If the patient's symptoms are glucocorticoid responsive, it becomes imperative to rule out causes of pruritic dermatologic disease first! Therapy for psychogenic alopecia, once all medical causes of pruritus have been ruled out, is focused on environmental management, behavior modification and behavior modifying drugs.

Infectious Folliculitis

If the hair follicle becomes inflamed because of any of, the following infectious causes, bacterial folliculitis, dermatophyte or demodex mites then the hair shaft from that infected follicle will fall out. The alopecia is typically multifocal and patchy in its distribution. Lesions of alopecia can vary in size and are not usually symmetric. Superficial bacterial folliculitis often causes a moth eaten appearance to the hair coat. The hair often epilates easily so check the margins of the lesions. Prognosis for hair regrowth is good since permanent follicular destruction (scarring) does not usually occur if lesions have been superficial.

Genetic Causes of Alopecia

Congenital hypotrichosis

Is rare and characterized by the absence of a hair coat at birth or loss of hair coat in the first month of life. Hypotrichosis can be localized or generalized in its distribution. In some cases characteristic changes for ectodermal, dysplasia such as abnormalities of the claws, dentition or lacrimal glands are also present, which are. The veterinary literature contains rare reports of congenital hypotrichosis in the Birman[2] , Siamese[3], Burmese[4] and Devon Rex[5] breeds. In these reports, affected kittens were born hairless or had a fine downy coat that was lost in the first few weeks of life. In the Birman cat, congenital hypotrichosis with short life expectancy (CHSLE) has been well characterized and is a non-mouse animal model for severe combined immune deficiency (SCID)[6]. Affected Birman kittens have a mutation in (FOXN1) an important transcription factor for development of both epithelial cells in the thymus and the hair follicle. Affected kittens are hairless or may grow sparse, shortened, fragile hair coats. The hairless skin develops excessive skin folds and a greasy keratinization disturbance[6]. A genetic test is available through AnimaLabs© (brand of InovaGen Ltd, Croatia) that can be used to screen breeding animals for carrier status for the FOXN1 mutation.

Hair Coat Changes as Breed Specific Traits
There are cat breeds such as the Sphynx cat, Peterbald, Donskoy and Kohana characterized by congenital hypotrichosis [7]. Affected cats vary from hairless to having thin, short fine coats. Sphynx cats are homozygous for an autosomal recessive hairless allele (hr) that results from a mutation in the gene Keratin 71 (KRT71)[7]. Keratin 71 is a type 2 keratin in the inner root sheath and Sphynx cats have abnormal inner root sheaths resulting in small, kinked hair follicles and misshapen, narrow diameter hair shafts[8]. The Donskoy and Peterbald are both autosomal dominant hairless breeds originating from Russia with yet unknown mutations for hypotrichosis[7]. The Kohana is an autosomal dominant hairless breed originating from Hawaii that also lacks vibrissae[7].

The curly coat of the Devon Rex also results from a mutation in the KRT71 gene[7]. The curly coat of the Cornish Rex results from a recessive trait resulting from a mutation identified in the lysophosphatidic acid receptor 6 (LPAR6) gene that codes for a receptor that is important for hair growth and maintaining hair shaft integrity and normal texture[9].

Inherited Structural Hair Shaft Defects
Pili torti is a structural abnormality of the hair shaft characterized by a flattening and twisting of the hair shaft around its axis by 180-degrees10. Pili torti in cats leads to alopecia as the flattening and twisting of the hair shaft likely leads to shaft breakage11. There is one report of three Abyssinian cats with a unique abnormal change to whiskers and primary hair shafts12. Affected hairs have a swelling on the tip of the hair shaft or sometimes along the hair shaft that was described as onion-shaped. Clinically, if primary hair shafts are affected, the hair coat appears bristly and feels rough. Trichograms to evaluate hair shafts for these characteristic changes are necessary to make the diagnoses.

Endocrinopathies
Thyroid Hormone
Thyroid hormones are very important to the skin and help initiate the anagen phase of the hair follicle cycle[13]. Hypothyroidism results in cornification disturbances, an increase in telogen hair follicles and accumulation of glycosaminoglycan in the dermis[13,14,]. Clinically, this results in alopecia, a dull, dry hair coat, variable hyperpigmentation, scaling, and myxedematous changes. The normal barrier function of the epidermis is likely impaired in hypothyroid animals and consequently, recurrent pyoderma and otitis externa can occur in hypothyroid animals[14]. Spontaneous hypothyroidism in cats is rare. One reported case had similar clinical signs to dogs with a dull dry, hair coat that was lighter in color than normal and the cat had a puffy face[15] but experimentally thyroidectomized cats did not; they reportedly groomed less, developed matting and seborrhea but only focal alopecia on pinnae and pressure points[14]. A recent study identified seven cats with spontaneous hypothyroidism with six having bilateral goiter and four had hair coat changes[16]. Hyperthyroid cats can develop matting, seborrhea, increased shedding and over-grooming[14]. With chronicity, alopecia may develop with hypotonic, thin skin[14].

Hypercortisolism:
Excessive cortisol can cause a number of skin changes including inhibiting the initiation of anagen. Increased cortisol whether endogenous from hyperadrenocorticism or iatrogenic from administration of corticosteroids can also cause cornification abnormalities, inhibit fibroblast proliferation and collagen production and cause pilosebaceous gland atrophy. Clinically, excessive cortisol (endogenous or exogenous) results in alopecia, disturbances in cornification, dermal thinning and delayed wound healing. Naturally occurring hyperadrenocorticism is rare in the cat and skin lesions have been seen in about half of the reported cases these include alopecia, thin skin, increased susceptibility to bruising, scaling, and fragile skin[17].

Cutaneous Paraneoplastic Syndromes
A paraneoplastic syndrome is defined as either a disease or clinical signs or symptoms that develop distant from the site of a tumor and these signs result from the presence of the tumor or its metastasis, but are not the local presence of neoplastic cells. Paraneoplastic syndromes are often mediated by hormones, cytokines or growth factors released by tumors or as an immune response targeted against the tumor. The term paraneoplastic is thought by some to be an inappropriate term to use if the clinical signs are associated with neoplastic tissue producing more of the same substance it normally produces. Consequently, either diseases such as hyperadrenocorticism caused by an adrenal tumor or pituitary tumor is not considered paraneoplastic, although some review papers may cite it as an example. Paraneoplastic skin diseases represent a group of skin disorders that if recognized alert the clinician to underlying internal neoplastic disease. These syndromes are seen most commonly in middle-aged to elderly individuals.

Feline Paraneoplastic Alopecia
This rare, yet highly characteristic skin disease occurs in association with pancreatic adenocarcinoma. Affected cats develop precipitous, ventrally pronounced alopecia in which the skin appears very shiny and smooth but is not fragile. Some cats may also have dry, exfoliative, and shiny footpads often with concentric circular rings of scale. On necropsy, exocrine pancreatic adenocarcinoma with hepatic metastases is the most common tumor found but bile

duct carcinoma has been reported in two cases[18]. The disease affects older cats and the chief clinical complaint is often the acute and dramatic alopecia that affects the ventral trunk, medial aspects of the limbs and the ventral cervical region but can generalize. Remaining hairs will epilate easily. Secondary *Malassezia* infections are common and may contribute to why some affected cats groom excessively, potentially exacerbating the alopecia. Skin biopsies histologically reveal epidermal hyperplasia with marked follicular and adnexal atrophy. Any cat with a tentative diagnosis of paraneoplastic alopecia should undergo an abdominal ultrasound to evaluate for the presence of a pancreatic or hepatic mass. Temporary resolution of the cutaneous disease was reported in one cat after the primary pancreatic tumor had been removed; the lesions recurred with progression of metastatic disease[19].

Feline Thymoma-Associated Exfoliative Dermatitis
A rare, exfoliative dermatitis has been described in middle aged to older cats with thymomas[20]. The exact pathogenesis is not known but is thought to be an immunologic etiology potentially T cell mediated. Histologically it is similar to an erythema multiforme or graft versus host type of reaction. Skin lesions tend to begin on the head and pinnae but can quickly generalize to involve the entire cat. Generalized erythema and marked scaling are present. Secondary infections with bacteria and *Malassezia* may develop. Respiratory signs secondary to the cranial mediastinal mass may be present at the time of presentation but in most cases, skin changes precede any other systemic signs. Histopathology of representative skin lesions reveals a cell poor, hydropic interface with apoptosis (single cell necrosis) of basal cell keratinocytes. If detected and diagnosed, removal of the thymic tumor will lead to resolution of the dermatologic clinical signs[18.20,21]. A recent report describes a group of cats that had clinical and histologic features of this exfoliative dermatitis but had no concurrent thymoma; the cats were managed with immunosuppressive medications[22].

Feline Degenerative Mucinotic Mural Folliculitis
A rare, visually distinctive, presumptively immunological skin disease of cats characterized by striking clinical features. Diffuse, generalized alopecia of variable severity, facial skin (especially the muzzle) becomes alopecic, thickened, and swollen, bilaterally symmetric, highly characteristic thickening of the lid margins and narrowing of the space between the eyelids. The affected skin of the muzzle becomes waxy, and has a rubbery feel. Scaling and crusting may be present Alopecia commonly begins on the muzzle and neck, and as it becomes generalized, it remains most pronounced on the head, neck, and shoulders. Pruritus is a feature in some cats. Non-specific clinical signs of lethargy and weight loss may be present . Skin biopsies will demonstrate a degenerative mucinotic mural folliculitis. Prognosis is poor as cats are frequently poorly responsive to immunosuppressive therapy.

Alopecia areata
This disease is caused by a spontaneous immune-mediated attack against follicular antigens in the hair bulb. The head, neck and legs are the most common affected areas. Lesions can be localized, multifocal or generalized (Alopecia universalis). Alopecia is non-inflammatory and non-pruritic. Spontaneous resolution can occur. Because it is considered a cosmetic disease in animals immunomodulatory therapy is not recommended. Prognosis for complete hair regrowth is good as often self-resolves over months to years.

Other Causes of Alopecia:
Telogen Effluvium
Telogen effluvium Results when hair follicles are pushed into premature rest due to stressful healthy events such as pregnancy, lactation, severe illness, etc. Clinically a patchy to diffuse non-inflammatory alopecia develops 2-4 months AFTER the physiological stressful event. Biopsies typically reveal normal growing hairs because by the time the condition is observed clinically the hair follicles have started to resume anagen or the growth phase. No treatment required as the condition self-resolves.

Anagen defluxion
The alopecia appears within days to weeks after a physiologic stress or administration of a cytotoxic drug
Cicatricial Alopecia:
A term used to describe a scarring alopecia in which the hair follicles have been replaced by scar tissue. The alopecia is PERMANENT. Diagnosed by biopsy.

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Feline Regional Dermatoses: Skin Diseases that Target the Dorsal Muzzle, Footpads, or Sometimes Both

Catherine Outerbridge, DVM, MVSc, DACVIM (SAIM), DACVD

Introduction

Regional dermatoses are skin diseases that target specific areas on the cat's body. There are skin diseases that can target just the footpads or just the dorsal muzzle, sometimes only the nasal planum. In some cases, the skin disease causes lesions in both of these body regions and will have a more generalized distribution.

The appearance of the lesion, presence or absence of other skin lesions, and information from medical history (ex: seasonal flares, response to prior therapies, concurrent clinical signs) can all assist in prioritizing a list of differential diagnoses. In this presentation, we will focus on the unique features in each disease that can help prioritize the list of differential diagnoses for cats presenting with dorsal muzzle/nasal planum skin lesions, footpad lesions or both. As a wide variety of diseases can cause very similar appearing clinical lesions, performing a skin biopsy is often required to reach a definitive diagnosis. This is critically important when therapy has associated risks or presumptive treatment for one differential diagnosis, if incorrect, could exacerbate other possible etiologies.

Biopsying the Nasal Planum or Foot Pads

Performing a skin biopsy of the nasal planum or footpad will likely require general anesthesia or heavy sedation. For footpad biopsies, regional anesthesia with nerve blocks can also be utilized. A 4 mm biopsy punch is the most commonly used size. The best place to biopsy depends on the disease suspected and the type of lesions present. Biopsies of ulcerated lesions should include the edge of ulcerated and epithelialized skin and pathologist informed of biopsy selection. If there are clinically, similar lesions on other areas of the animal it might not be necessary to biopsy the nasal planum or footpads. If suspecting a neoplastic process, it is best to perform a shave biopsy rather than obtaining a punch biopsy, the latter could seed neoplastic cells into deeper tissue. Closure may not always be possible depending on diseased tissue friability. Consider also weight-bearing function and if possible, for footpad biopsies select a representative lesion that is in a less weight-bearing surface.

Skin Diseases Targeting Dorsal Muzzle

Skin lesions on the dorsal muzzle of the cat's face can present a significant clinical challenge, as there are a number of very different etiologies that can all cause skin lesions that target this area in the cat. In cats, ulceration is the most common skin lesion to involve the dorsal muzzle but crusting and alopecia can occur. The nasal planum is a specialized area of skin and diseases that involve the nasal planum may be restricted to only that region, but in some cases, the nasal planum is one of many areas affected by a given disease. As the nasal planum lacks hair follicles skin diseases that involve hair follicles would not be anticipated to cause lesions in this unique region. Etiologies include infectious (viral, fungal) requiring appropriate antimicrobial or antiviral therapy, sterile inflammatory requiring immunosuppressive or anti-inflammatory therapy, or neoplastic diseases where delays in making the diagnosis can affect prognosis

Superficial Infections

Dermatophytosis and bacterial folliculitis could cause dorsal muzzle lesions often multifocal partial to complete alopecia with sometimes scaling but typically the nasal planum would be spares as there are no follicles present in skin in that region. Dermatologic in-room diagnostics such as surface cytology, Wood's lamp and submission of appropriate samples for fungal PCR or culture should help make the diagnosis. Treatment involves appropriate topical therapy and/or systemic antifungal or antibiotic therapy when indicated.

Feline Herpesvirus Ulcerative Dermatitis

This viral disease typically involves the dorsal muzzle but lesions may extend to involve the nasal planum. Cats do not have to have concurrent ocular or upper respiratory tract signs. Histologically the lesion is a necrotizing, ulcerative dermatitis most often with a concurrent marked eosinophilic inflammation but the inflammatory pattern may be strongly neutrophilic in some cases. The presence of eosinophilic inflammation and the clinical appearance of the lesions make it difficult to differentiate from mosquito bite hypersensitivity. Unless intranuclear viral inclusions can be identified on histology, it is not possible to diagnose definitively the virus as the etiologic agent for the ulcerative dermatitis on histologic examination and.PCR has been shown to be a sensitive test to detect the presence of the virus within skin biopsies[1]. Treatment can include subcutaneous administration of alpha interferon (1,000,000 units/m^2, 3 times a week), oral famciclovir (famvir) (90 mg/kg) [2], and/or lysine.

Deep Mycoses (blastomycosis, histoplasmosis and cryptococcosis)
Deep fungal infections have been reported to cause dorsal muzzle/nasal planum lesions. Typically, there are other cutaneous lesions and other systemic clinical signs. Sporotrichosis can involve the nasal planum and dorsal muzzle; these are areas where traumatic introduction of the organism can occur. Diagnosis of any of the fungal infections is based on demonstration of the organism within biopsied tissue and/or fungal culture. Appropriate systemic antifungal therapy is indicated.

Feline Mosquito Bite Hypersensitivity
This is a predominantly facial, hypersensitivity skin reaction to mosquito bites. Typically, has a seasonal pattern to its occurrence and is more common in outdoor cats. Darker coat colored cats may be more at risk, as mosquitoes seem to prefer more pigmented areas on the face of cats[3]. Most common clinical lesions are small papules on the pinnae. However, an eruptive, erythematous, often well-demarcated lesion can develop over the dorsal muzzle and involve the nasal planum. Lesions start as papules that coalesce and become areas of alopecia with varying degrees of ulceration and exudation. Lesions are often pruritic. Histopathology of skin biopsy is strongly eosinophilic and can be indistinguishable from herpes ulcerative dermatitis. Definitive diagnosis would be supported by the resolution of clinical signs with avoidance of exposure to mosquitoes. Treatment with short courses of anti-inflammatory doses of corticosteroids may be needed in some cases.

Nasal Ulcerative Dermatitis of Bengal Cats
This is a unique disease restricted to Bengal cats, first reported in Sweden[5], it is more common in Europe but cases have been reported in the USA. Cats develop clinical signs in the first year of life with the nasal planum becoming scaly and dry and gradually progressing to hyperkeratotic, crusted and fissured. Pigmentation may be lost. A genetic predisposition seems obvious but the actual etiology is unknown, although response to topical or systemic immunosuppressive therapies suggests an underlying immunologic mechanism. Various treatments have been utilized including oral prednisolone, topical salicylic acid, and topical corticosteroids. Topical tacrolimus caused rapid resolution in 4 cats[4].

Neoplastic Disease
Damage from solar radiation may cause sunburn and actinic keratoses in cats with nonpigmented nasal plana. Lesions progress from erythema to crusts to ulceration and destruction of normal architecture of the nasal planum corresponding to a progression from actinic changes to carcinoma in situ (noninvasive carcinoma confined to the epidermis) to invasive carcinoma. Squamous cell carcinoma (SCC) of the nasal planum is common in the cat. SCC most commonly affects the nasal planum, pinnae, and eyelid margins of cats. It is usually a disease of older animals, with a mean age of 12 years in the cat. White-haired cats have 13.4 times the risk of developing SCC than other colored cats[5]. Many treatment options are available for superficial squamous cell carcinoma of the feline nasal planum, which include strontium-90 plesiotherapy, cryosurgery, radiation therapy, photodynamic therapy, and excisional surgery.

Skin Diseases Targeting Footpads
The foot pads of cats have thicker epidermis to protect against mechanical trauma in addition there are large fat deposits that act as shock absorbers. Despite that thickness, the footpads are still vulnerable to environmental influences or trauma. Hard or jagged surfaces can cause lacerations. Caustic or irritating substances can cause footpad lesions but typically, the less thickened epidermis of the inter-digital spaces will also be involved. Depending on the disease, skin lesions maybe elsewhere on the body or the footpads may be the only area affected. Animals with only footpad lesions may be presented for lameness rather than skin disease.

Plasma Cell Pododermatitis
This is a rare cause of footpad swelling, sometimes progressing to ulceration in cats. The initial lesion is a soft, uniform, swelling of footpads that progress in some cases to ulcerations. Affected pads can develop scaling with linear striae and with chronicity; pads often appear partially “deflated”. Discomfort and lameness is possible but is more typical if ulcerations have developed. Diagnosis is confirmed by biopsy. There are some reports of an association with positive FIV status so testing for the virus is prudent. Recommended treatments include doxycycline (10 mg/cat every day for 4 to 8 weeks[6]) or tapering course of immunosuppressive doses of prednisolone. Doxycycline capsules or tablets should have 6 cc of water administered following oral administration to ensure that the medication enters the stomach and does not remain for any time period in the esophagus where it can cause esophagitis and stricture formation.

Eosinophilic Granulomas
These eosinophil rich lesions develop as a reaction pattern in cats with underlying allergic skin disease although it is recognized that some individuals may have genetic tendencies to form eosinophilic granulomas with no appreciable association with underlying hypersensitivities. Rarely, these lesions can involve footpads causing swelling and

occasionally ulcerative lesions. More often, they cause pink to orange linear lesions on caudal aspect of hind legs, or nodular lesions in the oral cavity. Some cats can develop a localized swelling on the chin with an eosinophilic granuloma, giving the cat a pouting chin appearance. The cat is often young (1 to 3 years). Biopsied lesions demonstrate: large foci of eosinophils and 'altered' collagen (actually normal collagen coated with eosinophil-derived debris) & palisading granulomas - macrophages, giant cells. Treatment includes evaluation for possible underlying allergies, corticosteroids, or cyclosporine in more refractory/persistent cases.

Cutaneous Horns
These keratinous proliferations occur on footpads and occasionally on the nasal planum. They can be associated with FeLV infection and in those cases, cats often have multiple paw pads affected and develop multiple cutaneous horns. Affected cats can present for lameness. Cutaneous horns have been reported to occur within skin lesions caused papillomavirus, actinic keratosis, squamous cell carcinoma [SCC] in situ, SCC, keratinizing acanthoma[7]. Solitary cutaneous horns should be biopsied for underlying neoplastic or preneoplastic causes especially if the horn is arising from a proliferative lesion. Screening for FeLV status is warranted in cats presenting with cutaneous horns. Diagnosis of FeLV related cutaneous horns is confirmed with a positive FeLV status and skin biopsy. Immunohistochemistry can demonstrate the presence of the virus within a skin biopsy. They can be idiopathic and if lameness is not present then lesions can be monitored or ignored. The conical horn itself, can be removed by trimming, however, they will typically regrow. Horn removal to prevent regrowth requires excision that includes removing the base if it is possible to do so without creating a large paw pad defect.

Feline Paraneoplastic Alopecia
There is an association with pancreatic adenocarcinoma in cats and a bilaterally symmetrical, strongly ventral distribution of alopecia in which the skin appears to appear very shiny and almost glisten but is not fragile. Some cats may also have dry scaly or fissured footpads. Secondary *Malassezia* infections are common. Diagnosis is confirmed by skin biopsy and abdominal ultrasound. Temporary resolution of the cutaneous disease was reported in one cat after the primary pancreatic tumor had been removed; the lesions recurred with development of metastatic disease[8].

Cutaneous Xanthomas
Cutaneous xanthomas are rare and occur when there is an underlying hereditary defect in lipid metabolism, or acquired dyslipoproteinemia. These skin lesions result from the accumulation of lipid-laden macrophages within the dermis. Feline cutaneous xanthomas may develop in cats with hereditary hyperchylomicronemia, megestrol acetate induced diabetes mellitus or naturally occurring diabetes mellitus. Apparent idiopathic cases of xanthomas with no identifying underlying metabolic or hormonal disturbance have been reported. Often, affected animals are consuming a diet rich in fats or triglycerides at the time they develop lesions.

Clinically, cutaneous xanthomas present as multiple pale yellow to white plaques, papules or nodules with erythematous borders. They are often located on the head, particularly the preauricular area or pinnae. Lesions can develop in paw pads and over boney prominences on limbs Lesions may bruise readily and larger masses may in rare cases ulcerate and exude inspissated necrotic material[9]. Cats with inherited hyperchylomicronemia may also demonstrate peripheral neurologic signs due to nerve compression from subcutaneous xanthoma formation. Histologic evaluation of skin biopsies reveals large foamy macrophages and giant cells. Serum biochemistry evaluations for diabetes mellitus, hypercholesterolemia and hypertriglyceridemia should be obtained. Feeding of a low-fat diet and identification and correction of the underlying disturbance in lipid metabolism is needed for patients that have had cutaneous xanthomas identified.

Metastatic Lesions from Pulmonary Adenocarcinoma
Primary pulmonary adenocarcinoma in cats can metastasize to the distal phalanges of digits. It does not target paw pads themselves but does cause distal phalangeal swelling. Cats will sometimes present with digital swelling that is visible to the owner or lameness. Typically, multiple digits on different paws are affected. Cats may have no respiratory signs so it is important to obtain foot and thoracic films in all cats with distal digital lesions.

Skin Diseases that Often Target Both Dorsal Muzzle and Footpads
Some of the above, discussed diseases can occasionally cause lesions on the dorsal muzzle and foot pads although one region is more likely to be affected than the other is. This includes mosquito bite hypersensitivity where in rare causes footpads can also be affected, or cutaneous horns, which can occasionally in cases of FeLV involve the nasal planum as well as footpads or might occur on the nasal planum secondary to a neoplastic or pre-neoplastic lesion.

Pemphigus Foliaceus (PF)
Pemphigus foliaceous is the most common autoimmune skin disease in the cat. Clinically PF is a pustular and crusting disease that occurs when there is an immune mediated attack against desmosome proteins responsible for

linking one keratinocyte to another. In a recent retrospective study of 49 cats, all cats had crusting lesions, 78% had alopecia, 73% had erythema, 61% had erosions or ulcerations and 22% had pustules present[10]. Skin lesions are often symmetric and in the majority of cats, two or more body regions are affected. The most commonly affected sites in cats with PF are the face and head including pinnae with lesions present in these areas in over 80% of cats[10,11]. The nasal planum is involved in 25-50% of affected cats and the feet were involved in 50 to 75% of cases[11]. The claw folds are often involved in reported cases (50 to 75% of cats) and about 15% of cats in one review had only claw fold lesions[11], So this is an important site to examine if suspecting PF in a cat .Paw pads themselves are only reportedly involved in 37 to 20% if PF cases[10,11]. When pads are involved lesions are often most obvious around the margins of the footpads.

Cats may be pruritic because of the PF lesions and they can have systemic signs of lethargy, diminished appetite or fever present. Possible association with drug administration has been reported in cats developing PF so reviewing medication history is important. Majority of cats have a leukocytosis with a neutrophilia present on CBC and 25 to 40% had anemia, hyperproteinemia and hyerpglobulinemia[10].

Diagnosis is based on skin biopsy of representative lesions. Ideal lesions to biopsy are intact pustules or very adherent crusts. Cytology of pustules or sampling underneath a crust may reveal presence of acantholytic cells which can increase evidence for the diagnosis. In retrospective studies, acantholytic cells were found cytologically in 19% of cases while acantholytic cells were seen on histology in 90 to 100% of cases.

Treatment involves immunosuppressive therapy with glucocorticoids (systemic and topical), chlorambucil or cyclosporine or combinations of these drugs. Corticosteroid monotherapy was sufficient to induce complete remission in the majority of cats in a recent study[10]. Disease flare-ups are common, reported in a literature review to occur in 45% of cats, often following a dose reduction[11]. The management of feline PF has an impact on Quality of Life (QOL) of both cats and owners[10]. Owners cited receiving/administering medications and attending veterinary appointments were a stress on their cats and that financial and time commitments were a source of stress for them[10].

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American Association of Feline Practitioners
2023 Spring into Feline Medicine ● April 30, May 10 & May 20

The Do's and Don't's of Trauma

Steven Berkowitz, DVM, DACVECC

Introduction

One study found that 11-13 percent of all admissions to tertiary veterinary centers are trauma related. Furthermore, trauma was the second leading cause of veterinary patients under one year of age, behind only infections, and similarly, the number two cause of death in patients over the age of one year behind neoplasia. As such, this represents a huge cohort of patients seen at many specialty hospitals across the country, and large populations of these patients have profound morbidity and mortality. The purpose of this lecture is to help us understand how to best help these patients in their time of need, and reduce creating iatrogenic, comorbid factors lending to their disease process.

Shock

By definition, shock is a state wherein the oxygen delivery (DO2) is not meeting the patient's oxygen consumption (VO2,) which leads to a state of cell dysfunction. If this dysfunction is not corrected, this can lead to cell death, progressing to organ failure, and ultimately could lend to patient death. In general health, the body is able to meet oxygen demand under varying degrees of stress and provide adequate cellular energy. However, in certain circumstances, called the "critical DO2," the delivery of oxygen is no longer sufficient to the demand of the tissues (VO2) and this leads to an anaerobic environment. Once this happens, these cells are essentially in a dire state of energy deprivation, or "shock."

Types of shock

Hypovolemic	Loss of circulating volume
Cardiogenic	Failure of blood flow (forward/backward)
Distributive	Loss of systemic vascular resistance
Metabolic	Altered cellular metabolic function
Hypoxic	Reduced oxygen content in blood

The way we address these types of shock are often very different from one another, however there are certainly instances wherein they overlap. For the scope of this lecture, we will focus mainly on hypovolemic and hypoxic shock; though one will notice occasionally other types will be intimately linked. The essential aspect to addressing hypovolemic shock is going to be to restore the circulating blood volume of our patients. This can be done in a variety of ways including crystalloids, colloids (including blood products,) and hypertonic or hyperosmolar substances. The circulating blood volume of an individual animal varies greatly, but generally we speak of a cat's to be 45mL/kg, and their "shock doses" being 60mL/kg. In states of shock, we need to ensure that we are at least meeting that demand, yet being care not to exceed it over-aggressively. Many studies over the years have shown that "overhydration" can lead to reduced DO2, and reduced cellular function, and in these already compromised patients, this could be catastrophic. Bolus therapy should be tailored for the individual patient and reassessed constantly whilst treating. As such, do not deliver the full "shock dose" of fluids, but rather do ¼ of it, and then reassess your patient's status. The bolus should be relatively rapid, 15-20 minutes, so to provide rapid intravascular volume, as opposed to a slower rate lending to interstitial fluid delivery. This is in essence the difference in treating perfusion versus hydration, for which our acute trauma patients are rarely in need of the later.

Monitoring of perfusion and shock

Often the best way to assess a patient's perfusion is via your physical exam! If they have a rapid capillary refill time, that leads you to believe they are in hyperdynamic shock and will need intravascular volume support. If they have poor or bounding pulses, that similarly often is a reflexion of shock. Your pulse pressure is determined by the difference in systolic pressure ("driving pressure,) minus diastolic pressure ("residual volume/pressure,") and large gaps between these values will lead to changes in palpable pulses. If the pulses are very weak, this may represent that the systolic pressure is also lacking, and may be enhanced by increasing your circulating blood volume. There are some papers that cite if you can "feel" a pulse, the mean arterial pressure is nearing 60mmHg, however, this has not been a consensus amongst other authors, so apply that information with caution. If you have access to arterial blood pressure monitoring, this will be your "gold standard," however non-invasive measurements (doppler, oscillometric, and plesthymography,) are still adequate alternatives to determine your perfusion pressures. A relatively easy way to monitor DO2 versus VO2 is to look at lactate values. In an aerobic environment, your cells will have adequate energy to function, however when that is lacking, your pyruvate cycle is altered, and lactate, a byproduct of anaerobic metabolism, will rise ("Type A" hyperlactatemia.) The more persistent the anaerobic

conditions are, the higher the levels may rise, and the longer they may persist. As such, if your patient has a very high lactate level, this is often a good indicator of shock. Those patients in which their lactate levels are brought back down into the normal range, or at least trending that way, have improved outcomes. Some older studies found that when the lactate was normalized within the first 6 hours of shock identification, the mortality was significantly reduced. At the current time, there are several machines that can evaluate point-of-care lactate, including individual strips very similar to the way we use glucometers. Some of the more invasive measurements include central venous pressures, monitoring urinary output, and even central venous oxygen saturation. In adequate DO2 to VO2 ratios, one would use approximately 25% of the O2 delivered to the tissues, and if you measure the oxygen saturation at your pulmonary artery compared to your aorta, 75% of the arterial oxygen concentration would still be there – when you have <70%, that likely indicates that your consumption (VO2) is outweighing your delivery (DO2.)

Medication Decisions

Pain control in traumatized patients is paramount to their stabilization – if they are in pain, they are stressed, which raises cortisol and will affect the physiological response to inflammation and as such, this must be dampened down. Ideally, a pure mu agonist should be used so that you can reverse it if needed. If that is not an option, partial agonists are reasonable second options. Never give non-steroidal anti-inflammatory pain medications to a shocky/hypovolemic patient. The arachodonic acid cycle provides a map of what cytokines are potentially blocked by these medications. Namely, your cyclooxygenase (COX) suppression will reduce the protective mechanism that prostaglandins provide. In times of reduced circulating blood volume, prostaglandins will increase renal afferent flow to protect the kidneys to prevent acute kidney injury (AKI.) They will also increase the amount of mucus being made in your stomach to prevent excessive irritation by the hydrogen atoms being liberated in the GI tract during stress, as well as increased blood flow to the gastrointestinal tract. As such, blocking this protective mechanism could increase risks of acute kidney injury and multi-organ dysfunction syndrome (MODS.) Finally, we know that COX inhibitors can reduce the platelets ability to form clots, and so we are also potentially inhibiting thrombus formation in a bleeding patient. Furthermore, steroids are also contraindicated for the same reason, however have also been shown in many peer reviewed papers that they do not improve morbidity or mortality in general trauma, or in traumatic brain injury (TBI.) In fact, they may worsen the outcome in TBI patients. Other options including lidocaine constant rate infusion, NMDA inhibition (ketamine/amantadine,) gabapentin/pregablain, as well as many other analgesic therapies that are less detrimental to perfusion can be considered in the traumatized or any patient in shock. Similarly, alpha 2 blockade, phenothiazines, and any medication that has the potential to reduced perfusion and vascular tone should be avoided in an unstable or cardiovascularly compromised patient. Appropriate antibiotics selection should also be made on an individual basis, and not need be used in blunt force trauma, or other scenarios wherein there is not a source of contamination. In the cases which there are concern for breach of the defenses, the route and spectrum of activity should be focused, rather than just broad coverage.

Damage Control

As noted above, in a patient already with reduced perfusion and inadequate DO2, all therapy should be guided to avoid anything that would further this negative energy balance. This is a theory called the “second hit” to the body. Anesthesia can reduce perfusion, blood pressure, alter immune response and have very similar sequele to shock, and should be avoided at all costs until the patient is more stable for a procedure. Thusly, unless absolutely necessary to save the patient’s life, any anesthetic procedure should be delayed until the patient is more stable. Clip and clean wounds, apply bandages where necessary, immobilize as needed, and provide a more declarative fix when it is safer for the victim. There are certainly instances wherein this is not possible (evisceration, large intrathoracic wounds, carotid artery laceration, other uncontrolled and life-threatening bleeding etc.,) however in many cases, these patients can benefit from 12-24 hours of stabilization prior to that “second hit.”

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2023 Spring into Feline Medicine ● April 30, May 10 & May 20

Feline Respiratory Emergencies: "Stat: Why is My Cat Panting?!"

Steven Berkowitz, DVM, DACVECC

Introduction

Feline respiratory emergencies are often rapidly evolving and are often difficult to assess due to dyspnea and patient anxiety. Knowing some tricks to help with diagnosis in the immediate presentation and how to stratify diagnostics are key to improved morbidity and mortality. The information provided below, as well as pure observation, will help improve diagnosis, comfort and prognosis of our feline friends.

Anatomy and Definitions

Dyspnea is, by definition, a physiological discomfort with breathing, which can be from chest tightness/pain, air hunger, or shortness of breath, that will lead to the patient trying anything it can to relieve this discomfort. This is very different than tachypnea or just rapid breathing. Usually, orthopnea, which is essentially changes made by patients to change their orthopedic position to help improve the act of breathing, is related to an attempt to relieve this physical pain associated with breathing. If you observe physical pain associated with breathing, this ought alert the clinician to rapidly assess for the cause of this distress.

The nasal and oropharynx are both sites wherein felines can have distress. Normally, obligate nasal breathers, cats will rarely breathe through their mouth. As such, if there is a partial/complete nasal obstruction, a cat may start to breathe with their mouth open. Usually in those circumstances, they are neither tachypneic or dyspneic, rather just using an alternate site for inspiration. The most common abnormalities in nasal cavities are going to be rhinitis, polyps, infections, or neoplastic growths. Signalmant will often help narrow the potential etiology of distress. Within the pharynx, you have the tonsils, larynx and epiglottis to consider. Tonsillar inflammation, trauma, abscess and neoplasia, especially squamous cell carcinoma should be considered in this region. These cats will not necessarily have tachypnea or dyspnea but will display altered inhaling and possibly heavy ptyalism on presentation. With trachea disease, you will also often see inspiratory alterations, leading to changes in their behavior to allow for improved drawing in of air, which can also be seen with abdominal breathing as well. This is in opposition to expiratory distress, wherein these cats tend to have more effort associated to exhausting volume. When that is observed, the clinician should focus on pulmonary parenchymal changes, including asthma, pneumonia, cardiogenic pulmonary edema, and other infiltrates. Restricted breathing patterns, consisting of choppier, or short/shallow breathing patterns, tend to be seen in those patients with pleura space disease. In cats, the most common ones would be pleural effusion, pneumothorax, thoracic wall trauma, or less commonly, neurogenic breathing. Focusing on the pattern of breathing will usually help the clinical team focus the gaze on which anatomical zone they need to address to help reduce patient distress.

Diagnostics

Often, as noted above, just watching the patient breathe, one can narrow the differential diagnosis of their patient, but not define the cause. When the pattern is restricted, if possible, POCUS (point of care ultrasound) should be initiated to assess whether there is free fluid, loss of glide sign (seen with pneumothoracies,) or if there are B-lines (pulmonary infiltrates.) This allows for rapid identification of pathology without needing to change the cats' position from wherein they feel most comfortable. If this is not available to you, thoracic radiographs are still a very useful tool in the arsenal. When radiographs are performed, ideally one would aim for three-view, but a simple lateral may be enough to start the therapeutic approach. If the patient has inspiratory distress, these diagnostics may not be as useful, and one should rely more on auscultation and palpation. If pulmonary edema is present, whether there is a heart murmur or not, a pro-BNP is very helpful. In patients with significant pulmonary edema and distress, if the test is "abnormal," cardiogenic pulmonary edema should be high on the list (albeit not 100% sensitive or specific.) As a screening tool, it is less helpful, but if abnormal in these conditions, it would not be inappropriate to assume CHF as a likely cause for respiratory distress. If there is pleural effusion, sampling the fluid is extremely important to help typify the cause (serious, hemorrhagic, exudative, purulent, chylous, etc.) Even if you will not have the sample back from the pathology lab immediately, looking at the PCV/TS and character of the fluid, as well as microscopically, will help guide both immediate and continued care. If upper airway is suggested by your physical exam, when possible, consider a sedated airwy exam when safe. Do not rush with diagnostics, for sometimes, just letting them relax in oxygen will allow for a much more stable patient. Do not be afraid to delay/stage diagnostics to help reduce morbidity to the patient.

Therapy

The use of sedation is often not only warranted but should often be part of the diagnostic process and stabilization of the respiratory feline. When they present with dyspnea, we must not forget that not only are they nervous, but often

painful, by definition of dyspnea. In our human counterparts, narcotics are contraindicated in respiratory distress due to depression of the respiratory center on the pons and medulla. Luckily, our feline patients are not nearly as sensitive. Butorphanol, a mixed agonist-antagonist opioid is extremely helpful in alleviating both parts of the distress. Often, a 0.2mg/kg dose (IM or IV,) will be enough to take the “edge off,” and allow for diagnostics and some degree of palliative care. This can be re-dosed fairly quickly if needed, especially at smaller doses as needed. If pleural effusion or pneumothorax is noted, this is often enough to allow for evacuation of the offender, with very little risk to the patient. If they are amenable to it, try and remove as much as is possible. This will allow for more comfort with the patient, but also allow the diagnostic team the ability to slow down and go over plans with the family. Often times, with severe pleural effusion, the simple act of paracentesis makes the patient markedly more stable and amenable for further diagnostics and transport. If cardiac disease is suspected, diuretics, most commonly furosemide at 1-2mg/kg should be initiated. Repeated doses of diuretics should be used with caution, for they may lead to severe dehydration, reduced renal perfusion, and worsening prognosis with non-cardiogenic pulmonary edema. The use of topical vasodilators, such as nitroprusside, should be used with caution, for they can also cause the same effect on the provider, or the pets family. Aerosolized therapy such as albuterol or fluticasone can be considered in an asthmatic, and injectable bronchodilators can also be considered with those patients, as well as those with pneumonia. When indicated, antibiotics that are concentrated in the pulmonary parenchyma or pleural space, should be chosen. Steroids should be used with caution, especially in feline patients that may have cardiovascular disease, for they may increase fluid retention and worsen outcomes. Additionally, long-acting steroids have been associated with significant hyperglycemia and transient diabetes, adding to worse morbidity.

Transfer

When the patient has been relatively stabilized, and is in need of more intensive monitoring and care, it is best to ship them to a facility that is able to support that. Ideally, if there is pleural effusion or air, removal of this should be attempted prior to transport. If this is not possible, consider contacting the hospital accepting the patient to alert them of the pathology prior to arrival. If the patient is no longer in overt distress, and it is deemed safe to send them back home whilst diagnostics are being reviewed, do not be afraid to afford that to the family either. When in doubt, always give all of the options to the patient’s family and allow them the help decide what is/may be best for them and their beloved cat.

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2023 Spring into Feline Medicine

American Association of FELINE PRACTITIONERS®

THREE-DAY **VIRTUAL LIVE CE EVENT**

Sunday, April 30th | Wednesday, May 10th | Saturday, May 20th

ALL TIMES ARE EASTERN TIME ZONE

Sunday, April 30, 2023

TIME	SESSION TITLE	SPEAKER	SPONSOR/PARTNER
12:00 - 1:00 pm	The Cat is Losing Hair: It's Not Allergies & it's Not Dermatophytes, Now What?	Dr. Catherine Outerbridge	
1:15 - 2:30 pm	Feline Regional Dermatoses: Skin Diseases that Target the Dorsal Muzzle, Footpads, or Sometimes Both	Dr. Catherine Outerbridge	
2:45 - 3:45 pm	The Do's and Don't's of Trauma	Dr. Steven Berkowitz	
4:00 - 5:00 pm	Feline Respiratory Emergencies: "Stat: Why is My Cat Panting?!"	Dr. Steven Berkowitz	

Wednesday, May 10, 2023

TIME	SESSION TITLE	SPEAKER	SPONSOR/PARTNER
2:00 - 3:00 pm	A Bright Future for Painful Cats: New, Improved, & Emerging Options for Multimodal Management of Feline Osteoarthritis	Dr. Erin Dresner	
3:15 - 4:15 pm	Feline Neurology: Pearls for Your Practice	Dr. Joane Parent	
4:30 - 5:30 pm	Improving Interpretation of Pulmonary Patterns	Dr. Lorrie Gaschen	
5:45 - 7:00 pm	FIP Updates: Optimizing Treatment Now & Into the Future	Dr. Sally Jayne Coggins	

Saturday, May 20, 2023

TIME	SESSION TITLE	SPEAKER	SPONSOR/PARTNER
12:00 - 1:00 pm	Management of Oral & Dental Pain	Dr. Heidi Lobprise	IVAPM
1:15 - 2:30 pm	Feline Stomatitis	Dr. Heidi Lobprise	
2:45 - 3:45 pm	Anterior Uveitis: Don't Miss The Big Stuff	Dr. Jessica Meekins	Dechra
4:00 - 5:00 pm	The Crystalluria Dilemma: When Should I Care About Crystals?	Dr. Julie Byron	ROYAL CANIN

A Bright Future for Painful Cats: New, Improved, & Emerging Options for Multimodal Management of Feline Osteoarthritis

Erin Dresner, DVM, MS, CVMA, DABVP (Feline)

New Insights into the Scope of Feline OA

Chronic osteoarthritis (OA) pain is one of the most common problems encountered in feline practice. Over 30% of all cats exhibit clinical signs of OA, and a stunning 90% of senior cats over the age of 12 years have radiographic evidence of degenerative joint disease.[1-5]

Despite the overwhelming prevalence of feline OA, less than 15% of affected cats worldwide receive a diagnosis. This is in stark contrast to dogs, who receive a diagnosis of OA nearly twice as frequently as cats.[6] One potential barrier to the diagnosis and treatment of feline OA pain is perceived client indifference, however one study revealed this may not be the case. When educated on the potential adverse effects of unmanaged OA pain, nearly 60% of American feline caretakers were interested in learning more about treatment options.

New Client Education Tools

Interactive Questionnaires

- Zoetis[7]
- Pain Free Cats[8]

Infographics for Social Media and Email

- Email - Zoetis
- Infographics - Zoetis

Updated Pain Management Guidelines

2022 AAHA Pain Management Guidelines for Dogs and Cats (Endorsed by AAFP)[9]
2022 WSAVA Guidelines for the Recognition, Assessment and Treatment of Pain[10]

Recent Refinement of Existing Validated Feline Pain Assessment Scales

The art of diagnosing and monitoring feline musculoskeletal pain has significantly progressed within recent years. We now have a total of four validated clinical metrology instruments (CMIs) specifically for use in cats with chronic arthritis pain: Feline Musculoskeletal Pain Index (FMPI), Musculoskeletal Pain Screening Checklist (MiPSC), Montreal Instrument for Cat Arthritis Testing-Caretaker (MICAT-C), and Client-Specific Outcome Measures (CSOM). In 2022, the widely accepted Feline Musculoskeletal Pain Index was refined, resulting in the development of the FMPI short form (FMPI-sf). The FMPI-sf is the first CMI to measure both pain assessment and treatment responsiveness.[8]

Novel and Refreshed Therapies for Feline Osteoarthritis Pain

Select Pharmaceutical Options

1. Solensia[12]
2. Liposomal transdermal gabapentin[13]
3. Pregabalin
4. Ketamine infusion
    a. Intravenous (5–15 µg/kg/min for at least 4 hours – anecdotal)
    b. Subcutaneous (0.5 mg/kg once every 2-3 days-weekly for a month, then once monthly – anecdotal)

Select Nutraceutical Options

1. Omega-3 Fatty Acids: 50mg/kg/day
2. Methylsulfonylmethane (MSM): 100–250 mg/day
3. Undenatured Collagen-II: 10–40 mg/day
4. Cannabidiol (CBD): 0.1–2 mg/kg twice daily

Select Non-Pharmacologic Integrative Therapies

1. Acupuncture
2. Laser Therapy
3. Pulsed Electromagnetic Therapy (PEMF)
4. Shockwave Therapy
5. Acoustic Wave Therapy

6. Regenerative Medicine – Stem Cell Therapy

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NOTES:

American Association of Feline Practitioners
2023 Spring into Feline Medicine ● April 30, May 10 & May 20

Feline Neurology: Pearls for Your Practice

Joane Parent DMV, MVetSc, ACVIM (Neurology)

This lecture presents a series of interesting facts and notable remarks accumulated over 40 years of neurological practice. The particularities of the neurological examination as it concerns the cat are discussed in relation to the diseases that affect the different anatomical parts of the nervous system, starting with the thalamocortex, then the spinal cord and finally the peripheral nervous system (PNS).

NEUROLOGICAL EXAMINATION:
The neurological examination is the cornerstone of clinical neurology. Its main objective is to localise the neurological lesion. Whatever the cause of the lesion, the neurological deficits observed with a specific nervous system region are similar. A stomach can only vomit regardless that it is a gastritis, a foreign body, or a tumour. It is the patient's signalment and history that allow the establishment of the differential diagnosis.

The neurological examination of the cat is like that of the dog as it concerns its various parts. However, there are some variations in the way the different tests are performed, as well as the way the cat expresses certain responses to these tests.

The different parts of the neurological examination include:

1. Mental status
2. Gait & posture
3. Cranial nerves
4. Postural reactions
5. Spinal reflexes
6. Nociception (+ back/neck pain)

MENTAL STATUS
Three observations:

1. The assessment of the mental status in the cat is often overlooked. If the cat's behaviour or history does not immediately raise a suspicion of a behavioural problem in the veterinarian, the cat's mental status is simply not questioned. It is assumed to be normal. This is especially true for the older cat. Problems such as hyperthyroidism, diabetes and renal failure are common in this category of patients. It is often assumed that the cat's mental status is directly related to its metabolic/endocrine problems. This is true, but if the medical problem(s) is(are) well controlled, the patient's mental status should not suffer. Consideration should then be given to the possibility of a structural disease such as a meningioma or other age-related cognitive changes.
2. The cat owner is often unaware that the animal has cognitive loss. When asked about this, their response is often quick and somewhat like this: 'My cat is normal, yes, he is a bit old, but apart from that, he is mentally normal'. It is important to make them understand how difficult it is to make a medical assessment of a cat's IQ. Cats are more independent than dogs, often living on the periphery of the family. Any change in their routine is significant if it is repeated over time. Asking the owner to rate their cat's behaviour on a scale of 1 to 10, 10 being normal, comparing the present behaviour with that of 3 weeks, 3 months, or a year ago, forces a reflection on the possibility of differences. If the family gives a number less than 10, it is then to question why a lesser number is given. An animal described as quieter, sleeping more, less active, is often part of the answers obtained. It is then the role of the veterinarian to decipher whether the abnormal behavior is coming from the thalamocortex or the brainstem.

   Regardless of the appearance of the animal's mental status in the clinic, it is crucial to thoroughly question the animal's behavior at home, in his environment if there is any suggestion of an abnormal mental status.
3. The assessment of the mental status is the most important step differentiating intracranial from extracranial disease. The cat is nervous and anxious in the clinical environment. He does not behave as if at home, even if he has had some time to relax. The assessment of the mental status is therefore largely based on history. The history, although often difficult to obtain, is essential and should be taken carefully.

BRAINSTEM vs THALAMOCORTEX
Mental status abnormalities originate in the brainstem, or in the thalamocortex (thalamus and cortex). A review of the basic principles of mental status follows.

A) BRAIN STEM: Arousal, wakefulness

The parenchyma of the brain stem is largely composed of the reticular formation, called the 'Ascending Reticular Activating System (ARAS)'. The term describes very well the function of this meshwork of fibers responsible for the state of arousal; its fibers ascend to the thalamus and cortex to wake it up. When affected, the animal's arousal is impaired. The cat becomes somnolent, lethargic, and if this progresses, the animal enters in a state of torpor and then coma. Somnolence is a state of arousal that cannot be documented in a clinical context. The adrenaline surge caused by the hospital environment means that changes in mental status, especially if subtle, go unnoticed. The somnolent cat behaves NORMALLY but he is quieter when left alone, unstimulated.

In cases of wakefulness abnormalities, cranial nerve deficits (III to XII) are ALWAYS present. The questioning of arousal should therefore always be done thoroughly when there are deficits in one or more cranial nerves. If a cranial nerve deficit is accompanied by a decrease in wakefulness, then the disease is intracranial, involving the area of the brainstem where the nucleus of that nerve is located.

The changes in arousal indicate whether the lesion is intracranial or extracranial, not the deficits in proprioception. Obviously if the latter are present, it is certainly a central nervous system problem, but proprioceptive losses are rarely observed with brainstem disease, compared to the frequency of decreased arousal. To note, if proprioceptive losses do occur, they will be seen in the assessment of postural responses and not the gait. Cats with brainstem lesions affecting the proprioception are not ataxic.

BRAINSTEM (Decreased arousal + Cranial nerve deficits)

Every single time a clinician is presented with a cat with a head tilt, or facial nerve paralysis, or other cranial nerve (III to XII) deficits, a thorough questioning regarding presence of somnolence in the home environment must be investigated. Even in cases where the cat is assessed as normal by the owners, a doubt should be kept as frequently, families have not observed any changes.

B) THALAMOCORTEX: Intelligence (‘IQ or Intelligence Quotient')

The combination of the thalamus and cerebral hemispheres constitutes the thalamocortex. It is the site of intelligence, of goal-directed behaviors. Obvious behavioral disorders, such as the cat circling, or the cat pressing against the wall, are rare. In most cases, the changes are subtle, especially if the disease is progressing slowly, or insidiously, as in meningiomas as examples. The clinician then is relying uniquely on the history to bring the behavioral changes into light. In these cases, the animal does not respond appropriately to environmental stimuli. There is cognitive impairment or a decrease in awareness. The cat may be described as deaf or blind, the family assuming there is a hearing or an ocular problem. It is always important to ask the family to give examples or actions of the cat that have led them to conclude that it is deaf or blind. The blindness of the cat that bumps into objects is the result of a thalamocortical disorder. The thalamocortex does not integrate what the eye sees. The cat blind due to a primary ocular problem does not bump into walls and objects. Its other senses become hyper-developed, and it compensates very well for the loss of vision. The same can be said for the apparently deaf cat. If there is bilateral inner ear problem, the cat should still behave the same way because its other senses take over.

It is much more difficult to decipher the history of the cat with cognitive problems. The cat is described as less active, less playful, sleeping more, sleeping more deeply, a description that is also present in the chronically ill cat. This is where the veterinarian's detective work is most difficult.

THALAMOCORTEX (Behavioral changes &/or Seizures)

The questioning for the presence of behavioral abnormalities is paramount in the cat experiencing seizure activity. Genetic/idiopathic epilepsy is rare in cats. Consequently, structural disease must be ruled out; this is done by ruling out presence of behavioral abnormalities. The temporal and frontal lobes have the highest propensity to cause seizure activity; these lobes are also concerned about behavior. Putting aside the behavioral changes, the neurological examination will be unremarkable. Since families are poor at observing behavioral changes, especially if insidious, magnetic resonance imaging (MRI) of the brain should be strongly recommended in any cat with acute onset seizure activity.

Meningiomas are frequent in cats. Most are supratentorial (sit on the thalamocortex). They may cause behavioral changes and seizure activity. The cat presented with behavioral abnormalities is not a problem as clearly, the lesion is in the thalamocortex. It is the cat presented with seizures alone that is problematic because beside seizures, there is nothing else, the family being so poor at observing changes. It is difficult in our domestic species to tell if the patient’s IQ has decreased of 5 points!

Facts regarding seizure activity strongly suggestive of structural thalamocortical diseases:
→ Acute onset of frequent seizures (as in viral, frequently self-limiting, encephalitis).
→ Changes in seizure type: focal or non-convulsive generalized seizures that progress into convulsive seizures over time.
→ Focal seizures (only one side of the animal is involved) that progress or not into generalized seizures.
→ Any cat > 10 years or older seizing for the first time.
The pattern of seizure (type and frequency) should not change over time in a patient with idiopathic epilepsy or epilepsy of unknown cause.

CRANIAL NERVES
It is always preferable to do the neurological examination in the examination room with the owner, the cat sitting on the owner's lap, the clinician kneeling in front of the patient.

The cranial nerve examination is all about subtleties. Counting from 1 to 12 is the best way to ensure that ALL 12 pairs of cranial nerves are evaluated. 'There is more missed from not looking, than not knowing'.

<u>The olfactory (I) and accessory (XI) nerves are not examined.</u>

As a review, the location of the cranial nerve nuclei is presented. Then the discussion focuses on those nerves where the author has observed particularities with respect to the cat.

THALAMOCORTEX:	I. Olfactory N.
	II. Optic N.
MIDBRAIN:	III. Oculomotor N.
	IV. Trochlear N.
PONS:	V. Motor trigeminal N.
ROSTRAL MEDULLA	V. Sensory trigeminal N.
	VI. Abducent N.
	VII. Facial N.
	VIII. Vestibulocochlear N.
CAUDAL MEDULLA	IX. Glossopharyngeal N.
	X. Vagal N.
	XI. Accessory N.
	XII. Hypoglossal N.

<u>Optic nerve (NC II):</u>
When we examine the optic nerves, we examine the entire visual pathways, from the retina to the optic nerve, optic chiasm, (with 70% of the fibers crossing contralaterally), optic tract, optic radiations and finally to the occipital cortex or visual cortex. The menace response is the test that assesses this pathway.

MENACE RESPONSE:
This test, simple at first sight, is one of the most difficult to master. It is not a reflex but a response because it requires cortical integration. The airflow must be minimized to avoid distorting the results by stimulating the trigeminal nerve, which is responsible for the facial sensation. The cat's vibrissae can be very long; stimulation should be avoided. It is recommended to make the menace gesture touching the eye a few times, so the cat 'learns' that it will be touched each time. The response is learned within a few seconds. Then the movement is repeated rapidly, alternating from one side to the other, with a brisk yet short motion about 1 foot (30 cm) from the cat's head. Since fiber crossing is 70%, a lack of response on one side locates the lesion to the contralateral thalamocortex if the pupillary light reflexes are present.

Since the menace response assesses the thalamocortex as part of the visual pathway, the emotional state of the patient greatly influences the results obtained. In the clinical setting, the response could be bilaterally absent due to the patient's fear or fright. The lack of response should obviously be bilateral in these cats. This apparent lack of response is much more common in cats than in dogs. Whenever the menace is absent, it is good to repeat the test at the end of the neurological examination to insure it was real. By then, the patient is getting more used to be manipulated.

The menace responses evaluate the vision, the facial nerve, and the cerebellum. When absent because of cerebellar disease, cerebellar signs are obvious.

Oculomotor nerve (NC III):
The oculomotor nerve is responsible for A) pupillary constriction and B) eye movement. Four items are assessed with respect to the pupils during the oculomotor nerve examination:
1) Pupil size at rest, before light stimulation
2) Pupil symmetry
3) Funduscopic examination (retinas and optic discs)
4) Pupillary light reflexes

1. The size of the pupils at rest is important. In the clinical setting, the pupils should be larger than normal secondary to the adrenaline surge experienced by the animal. Assuming there are no ocular problems, small pupils in a patient with cognitive loss suggest the possible presence of a lesion in the thalamocortex causing disinhibition of the oculomotor nerves.

2. The assessment of pupillary symmetry is more difficult in cats because of the large (70%) overlap of retinal projections at the optic chiasm. Before diagnosing the presence of anisocoria, ensure the light source is equal in both eyes.

3. It is always appropriate to assess the retinas. The optic nerve is a brain projection and therefore, by extension, brain disease can lead to retinitis or neuritis and vice versa. Fundus examination is part of the neurological examination.

4. As described above, the stress on the patient during the clinical examination causes mydriasis. A transilluminator is required for the assessment of pupillary light reflexes. Only this instrument provides sufficient stimulation to overcome stress-induced mydriasis. The highest concentration of cones and rods is located lateral to the optic disc. Therefore, the light beam is directed obliquely, mediolaterally. As the pupil becomes smaller, the beam is positioned more and more at right angle to the pupil to allow the light beam to pass through the center of the pupil. Do not hesitate to come very close to the eye. The pupils should constrict significantly.

Large pituitary masses at the base of the skull often causes bilateral absence of the menace responses (from compression of the optic nerves cranially) and mydriasis (from compression of the oculomotor nerve caudally).

Oculomotor Nerve (NC III), Trochlear Nerve (NC IV), Abducens Nerve (NC VI):
These nerves form a functional unit. They are responsible for the movements of the eye. As the pupil of the cat has an oblong shape, it is possible to observe a strabismus caused by damage to cranial nerves IV or VI. In these cases, the eyeball turns on its main axis to one side or the other. If the pupil was round, such a strabismus could not be easily diagnosed.

Strabismus is rarely observed.

Trigeminal nerve (NC V) motor and sensory:
There are three branches, namely the ophthalmic, maxillary, and mandibular branches, which are evaluated by the palpebral reflexes. Touching the medial cantus evaluates the ophthalmic branch of cranial nerve V and the facial nerve (NC VII) because it causes ipsilateral eyelid closure. Touching the lateral cantus evaluates the maxillary branch of nerve V and nerve VII. Touching the base of the ear evaluates the mandibular branch of nerve V and nerve VII. The stimulus must be stronger (use the finger) when evaluating the mandibular branch.

The mandibular branch of the trigeminal nerve is mixed. Its motor portion controls the muscles of mastication while the sensitive portion is responsible for the sensation of the skin above the mandible and the mandible itself, bones, and teeth.

Stimulation of the nasal septum evaluates the sensitive portion of the nerve and contralateral cortical integration. If palpebral reflexes are present, the response to nasal septum stimulation evaluates the thalamocortex. As observed with the menace response, the frightened cat may have an absence of response even when the stimulus is relatively strong (wooden end of the cotton tip). It is worth repeating this test at the end of the examination if there was ambiguity.

This test assesses whether there is a nociceptive asymmetry between one side and the other. Start with a very weak stimulus, gradually increasing the intensity of the stimulus until you are certain there is, or not, a difference. The vibrissae are touched first, then the upper lip and, if necessary, the external nostril and finally the nasal mucosa. It is

important to ensure that the stimulus is the same on each side and that the same place is touched and with the same angle. The nostril is not as sensitive as the nasal mucosa. This test demonstrates how subtle the deficits can be.

Facial Nerve (NC VII):
Observe the position of the ears, the size of the palpebral fissures, the openings of the nostrils, and the corners of the mouth. The difference can easily go unnoticed if the observation is not rigorous.

Vestibular Nerve (NC VIII):
The cochlear portion is not assessed. Electrodiagnostic is necessary to evaluate the auditory pathways.

The best way at assessing presence of a head tilt is to draw an imaginary line between the two eyes. The line should be perfectly horizontal. It is best to make this observation while the animal is walking freely in the examination room. The head tilt can be very subtle. The severity of the head tilt does not correlate with the severity of vestibular ataxia, especially in central nervous system (CNS) disorders.

Bilateral vestibular disease may have a very mild head tilt on the more affected side.
Cranial nerve IX, X and XII are rarely affected. Evolution has made this part of the brainstem resilient because it is essential to survival.

Glossopharyngeal (NC IX) and Vagal (NC X) nerves: functional unit:
These nerves are responsible for the function of the pharynx (choking on eating or drinking) and the larynx (noisy breathing, voice changes, snoring). Their evaluation is based on history.

Hypoglossal nerve (NC XII):
This nerve is responsible for the function of the tongue. The examiner observes for symmetry, and presence of atrophy, deviation and fasciculations (usually brainstem lesion).

GAIT & POSTURE:
The challenge in assessing the gait is to get the cat to walk in the hospital or clinic environment. Most are frightened and remain immobile. It is sometimes useful to use the carrier as a subterfuge, leaving it on the floor with the door open and moving it when the animal tries to hide in it.

If a gait abnormality is the reason for the presentation and the animal refuses to walk, it may be necessary to send the animal home and ask the family to video the abnormalities observed.

It can also be suggested when the owner is taking the appointment.

A systematic approach greatly aids the assessment. The examiner mentally answers the following questions:

1. Is the cat ambulatory?
2. If the cat can walk, is the gait normal?
3. Which limb(s) is/are affected? One limb only? Pelvic limbs only? All four limbs? Ipsilateral limbs?
4. Is ataxia present?
5. If there is ataxia, what type is it? Vestibular? Cerebellar? Proprioceptive?
6. Is there a postural abnormality (head tilted, arched back, neck curvature, etc.)?

Principles to remember:

- Lower motor neuron (LMN) deficits are visible at the walk.
- Examining the gait carefully as the cat walks freely around the room cannot be emphasized enough. Have your cell phone ready. It avoids waiting for the cat to accept to walk again. When looking at the video, use the slow motion to exacerbate the abnormalities.
- Bilateral vestibular diseases are best diagnosed with the animal walking about the room. The exaggerated movements of the head are characteristic.
- The withdrawal reflex is difficult to interpret, again emphasizing the need to assess the patient's gait.
- Involvement of the tail always implies vertebral canal disease.

POSTURAL REACTIONS: PROPRIOCEPTIVE POSITIONING & HOPPING
Postural reactions are of little value in locating the lesion. However, when performed well, they are invaluable in the assessment of proprioception, especially in the case of cortical disorders.

Proprioceptive positioning or paw placement is often difficult to assess in cats, as they do not allow their paws to be touched. This test is then replaced by tactile lateral placing. For the assessment of the right thoracic limb, the animal

is held in a lateral position in the arms of the examiner and against the examiner, with the head to the left of the examiner. The examiner, with his right hand, holds the cat's left thoracic limb under the cat's thorax. With his left hand, the examiner blocks the cat's vision while bringing the side of the cat's right thoracic paw against the edge of the examination table. The cat should immediately put its paw on the table. The test is repeated for all four limbs.

If the cat allows his paw to be knuckled over, do the test VERY SLOWLY, supporting the cat's weight. The more proprioceptors are captured doing the test and the least useful it is. If the test is done rapidly with the animal's weight on his paw, subtleties are missed.

Hopping. Each limb is hopped laterally. It is sometimes necessary to put the full weight of the animal on one limb to obtain the cooperation of the patient. It is a good idea to do the test slowly, if the cat allows it, as it acts as an evaluator of proprioception. The time it takes for the animal to hop on its limb indicates the quantity of proprioceptors that must be recruited before a response is obtained. This test is not done medially. Although it is said that subtle changes are more easily highlighted in this way, this is not the author's experience. Done medially, the cat tends to be carried along by the examiner.

SPINAL REFLEXES

The reflexes examined are:

1. Patellar reflexes
2. Withdrawal (flexion) reflexes of all four limbs
3. Thoracic limb extension reflex (can the animal stand? Can you raise extensor tone)
4. Perineal reflex
5. Cutaneous trunci reflex

The author finds it easier to have the cat held by the owner on his/her lap. One hand of the owner is holding the cat's rear end while his/her other hand holds the cat by the chest. The cat is then standing on the owner's lap, back against the owner, limbs facing the examiner. It is easier for the owner to hold the cat this way rather than attempting to immobilize the cat in lateral recumbency on a table. The veterinarian does not always have the luxury of having an assistant to help.

PATELLAR REFLEX:

The patellar reflex (tendon or monosynaptic reflex) is elicited by hitting the patellar tendon. An extension of the stifle is observed when the patellar tendon is struck. The limb must be in a relaxed position. To induce the reflex, the tendon is first palpated with one hand while the other hand is positioned against the plantar surface of the cat's paw. While keeping the finger on the tendon, the limb is flexed until the tendon is under tension. The limb can be moved forward or backward if necessary to increase the tension in the patellar tendon. The tendon is then struck with a pendular motion with the handle of a neuro-hammer or the handle of a hemostatic clamp (the instrument should be less wide than the length of the tendon). If the limb is too tense, the reflex will not be induced. Keep tapping the tendon, like a pendulum, with a regular movement and the animal will relax over time. With tendon reflexes, the strength of the reflex is proportional to the force applied to the tendon. Sometimes the extension of the stifle is better felt against the hand than observed with the eye.

To better assess the patellar reflex in cats, it is sometimes better not to touch the limb at all.

The patellar reflex can be difficult to induce but is easy to interpret.

As the patellar reflex assesses the extension of the stifle, this assessment can also be done indirectly, with the cat standing and the examiner's hand under the limb. By 'teasing the limb' it becomes possible to induce extensor tone and even lift the cat off the ground with its pelvic limbs straight.

WITHDRAWAL/FLEXOR REFLEXES

Withdrawal (flexor) reflexes are difficult to examine objectively. In most of our patients, voluntary movements are present, and the animal can therefore inhibit the reflex. In diseases of the lower or upper motor neurons, there is a decrease in the strength with which the animal can withdraw its limb. The reflexes of the thoracic limbs can be used as a comparison for the pelvic limbs and vice versa depending on which are affected. The examiner assesses the force with which the animal pulls its limb and whether each of the limb joints flexes.

The withdrawal reflex is easy to induce but can be difficult to interpret.

Plantigrade stance:
Lower motor neuron signs are visible at the walk. The cat walking on his hocks has distal sciatic nerve deficits because there is no hock extension. Veterinarians are surprised at time to find good withdrawal reflexes in such a cat, but it is the extension of the hock that is not occurring. As a result, the flexor muscles have lost the antagonistic muscle mass. Moreover, if the animal has been plantigrade for some time, the flexion of the hock is stronger even if only from shortening of the tendons/ligaments.

THORACIC LIMB EXTENSOR REFLEX:
Thoracic limb extensor reflexes are best assessed by observing whether the animal can bear weight on its thoracic limbs. The triceps reflex is not performed due to its difficulty in being elicited in most normal cats as its tendon is too short. If the animal is non-ambulatory, the reflex is assessed by examining for the presence of extensor tone. *The radial nerve is responsible for joint extension of the thoracic limb, hence weight bearing, whereas the femoral nerve is responsible for weight bearing for the pelvic limb.*

PERINEAL REFLEX:
Touching with a cotton swab, or gently pinching the animal's perineal area, under its tail, assesses the perineal reflex. Avoid touching or grabbing the tail as this removes the surprise effect and the animal may then already reflex responds. The reflex is assessed on each side separately. The expected response is a downward contraction of the tail, which is more reliable and easier to observe than the contraction of the anal sphincter. To assess the motor part of the sphincter reflex, a rectal examination is preferred.

Tail avulsion:
Most of the spinal segments responsible for the function of the nerves of the hind limbs and sphincters are located within the vertebrae L5 and L6.

The cat's spinal cord (filum terminal) ends in the middle of the sacrum.

At this level, what we have in the canal are nerve roots, dorsal (sensory) and ventral (motor). The dorsal and ventral nerve roots unite to form a spinal nerve, which then become a mixed nerve. The union of the roots occur within the foramens. Consequently, the cauda equina is made of sensory and motor nerve roots. The meninges are attached to the bone around each of the foramina and are inelastic. During avulsion, the meninges of the sacral foramina bear a significant portion of the impact but are in most cases broken. With them, the dorsal and ventral nerve roots are partially or completely severed.

The anus is innervated by the pudendal nerve, which is derived from the spinal nerves S1, S2 and S3. The prognosis is guarded in the absence of anal sphincter sensation. Remember that the skin adjacent to the anal sphincter, where the hair changes direction, is innervated by the L7 spinal nerve. In tail avulsion, the L7 nerve roots are rarely affected. It is therefore important to pinch the skin with a small hemostatic forceps a little inside of the anus so as not to stimulate the skin innervated by the L7 spinal nerve, and falsely give a better prognosis.

Lymphoma (tail involvement = vertebral canal disease)

Tail involvement implies vertebral canal disease. A good example is lymphoma.

Lymphoma can be presented as cauda equina syndrome. In this case, the multiplication of the neoplastic cells compresses the nerve roots. The clinical signs of lower motor neuron signs affecting limbs, anus and tail predominate.

The cat presented with plantigrade stance in one of both hind limbs, and non-specific systemic signs such as decreased appetite or lethargy, should be investigated for lymphoma. These cats are often FeLV and FIV negative. The diagnosis is made by magnetic resonance imaging (MRI) +/- cytology of the affected roots.

The prognosis for this type of lymphoma is poor, even with chemotherapy. This may be because these animals are diagnosed at an advanced stage of the disease.

CUTANEOUS TRUNCI REFLEX:
The cutaneous trunci reflex is frequently absent in cats. This absence is meaningless. At times, it is partially or unilaterally present and yet there is no clinical vertebral canal disease.

NOCICEPTION (back/neck pain):
The pain response is assessed at the end of the examination to maintain patient cooperation. With experience, it is realized that it is not always necessary to examine whether the cat perceives pain as many clues are gleaned during the examination to inform the clinician of the presence of pain perception. In veterinary medicine, the terms 'deep' and 'superficial' should probably not be used because of the variation in the way animals' express pain. There is a decrease (hypoesthesia), increase (hyperesthesia) or absence (anesthesia) of pain perception.

The examiner should pinch the toe and not the skin between the toes, which often does not feel as painful. For pelvic limbs, the lateral toe is pinched for sciatic nerve assessment and the medial toe for the femoral nerve assessment. For thoracic limbs, stimulation of one of the toes is sufficient since the radial nerve innervates the dorsal part of the paw and the median nerve the palmar region.

When assessing pain sensation in the paralyzed animal, assess the toes first. If absent, stimulate the tail. Sensation in the tail disappears later probably due to its autonomic innervation and more resilient fibers.

Pain perception should be assessed in a quiet place with an animal that has had time to acclimatize to its environment. In severely affected animals, the pinching of the toes may only be a tingling sensation which, considering the cat's frightened state, will not cause a painful reaction.

BACK PAIN:
The examiner applies pressure along the spine from the upper thoracic region to the lumbosacral region. Do it gently and rapidly at first, increasing the pressure gradually. The cat may have a hunched back, but this posture is not as consistently observed in cats as it is in dogs, even when back pain is present.

Many normal cats do not tolerate lumbar/lumbosacral palpation. Nevertheless, the veterinarian should always ask if the cat is painful from the owner's point of view. Its historical presence should never be accepted at face value. Owners should always be asked to describe what it is about their pet's behavior that makes them think their pet is in pain. With back pain, there is often hesitation or refusal to climb up or down stairs, beds, or sofas. The cat may also have withdrawal behavior in the home environment.

CONCLUSION
The neurological examination must be done methodically and thoroughly with attention to details. In cats, the examination should be done rapidly to maintain the cooperation of the patient. The results of the examination should always be recorded in the patient's medical record. A neurological form is of great assistance. It serves as a "checkpoint" to ensure that all parameters have been assessed. Most importantly, it is an invaluable document in the follow-up and monitoring of progressive or prolonged diseases of the nervous system.

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American Association of Feline Practitioners
2023 Spring into Feline Medicine ● April 30, May 10 & May 20

Improving Interpretation of Pulmonary Patterns

Lorrie Gaschen, DVM, PhD, Dr.med.vet, DECVDI

Introduction

After performing a systematic review of the entire thorax, careful scrutiny of the lung can be one of the most challenging parts of analyzing a thoracic radiograph. Using a practical approach to determine if the lung is abnormal or not then deciding on whether the air space, the airway is important. Also important to realize is that most all diseases cross the borders of all parts of the lung.

Are patterns important?

The principles of the pulmonary pattern are important, but a lot of stress can be associated with trying to determine the correct pattern so that one can make the correct diagnosis. A better approach is to determine if the main opacity of the lung is in the air space or the airway. Most diseases are in one or the other. In between is the interstitium and the interstitium is often involved anyway. Pure interstitial disease is really only sure when structured nodules are present. Unstructured interstitial disease is often very difficult to diagnose as a sole abnormality. Determining if disease is in the air space or airway is the best way to set a course of action. By creating a best course of action based on which compartment is most affected and then re-assessing the radiograph at an appropriate time point following treatment is good medical practice.

The normal lung

The normal feline lung is rather lucent with few linear markings, mostly visible centrally. The periphery of the lung is almost devoid of vascular markings. Thinner body condition makes the lung look hyperlucent and bronchial and vascular markings may be more visible in the periphery. The opposite is true for obesity where the lung has a hazy interstitial appearance due to the opacity of superimposed fat. Both situations make the lung challenging to assess and emphasis on the clinical signs is important for interpretation.

Air space disease

The alveoli are filled with air and this allows the vessels and bronchial structures to be sharply marginated and therefore well visible. These structures are extremely small in the periphery of the feline lung and this is the reason the periphery is so lucent. When an increased opacity is identified, the first duty is to determine if it is effacing the border of any of soft tissue structure. The margins of the heart, pulmonary vessels, caudal vena cava and diaphragm should be scrutinized first. If any one or more of those margins are blurred, the pulmonary opacity is likely in the air space: it replaces air with soft tissue and the air no longer outlines soft tissue structures, making them less visible. Air space disease may be lobar. If the right middle lobe is homogeneously soft tissue opaque and is the only lobe affected, then atelectasis due to lower airway disease is the likely cause. Aspiration pneumonia is rare in cats and would only be diagnosed if there is a clinical history of vomiting or regurgitation. If the clinical history fits with best with increased respiratory rate and wheezing, then atelectasis is the diagnosis.

Other radiographic features of air space disease are air bronchograms, consolidated lobes with lobar sign, and patchy opacities that silhouette borders of vessels, heart and diaphragmatic contours. Lobar consolidation is when the entire lobe is homogenously soft tissue opaque and not reduced in volume, with our without air bronchograms. It is usually due to pneumonia, neoplasia or contusion. Atelectasis is collapse of the lobe due to pleural space disease or bronchial obstruction. The lobe is opaque and there is a decreased volume, and mediastinal shift of the heart to the affected lobe.

Common disease categories causing air space disease are pneumonia, edema, hemorrhage, atelectasis, infection, allergic inflammatory disease, and some neoplasia.

Multifocal, ill defined, patchy soft tissue opacities that obscure the airspace and vessels in their surrounding are often due to infection or edema. Fungal pneumonia and cardiogenic edema are the most common of these, but neoplasia and contusions also have this appearance. Histoplasmosis can also have a patchy ill-defined mixed or airspace pattern as can cardiogenic edema. Other causes of infectious pneumonia are mycobacterial, cryptococcal, blastomycosis, aspirgillosis, toxoplasmosis, paragonimus and aleurostrongylus.[1] Lipid pneumonia is less common but consistently seen in cats. Radiographic abnormalities in aleurostrongylus infection are dependent on severity and duration of infection. Early changes of bronchial thickening and small, poorly defined nodules progress to a generalized alveolar pattern in severe cases. After partial resolution of the alveolar pattern, an unstructured, patchy interstitial pattern develops.

Airway disease
Lower airway disease can appear radiographically normal or have varying severities of airway pattern. Tracing the trachea to the carina and then tracing each main bronchus of each lobe should be performed. Two-thirds of the way out from the carina, the visualization of the bronchial walls and vessels should slowly disappear. If larger numbers of branching structures are visible, then an airway pattern is present. However, clinical signs are not always present. The clinical signs of airway disease may wax and wane, but chronic airway patterns are persistent on thoracic radiographs, regardless of clinical activity. This is where reader bias can sway the importance placed upon the presence of an airway pattern, or even lead the reader away from other abnormalities due to tunnel vision. [2] Airway disease is usually due to allergic airway disease, asthma and heartworm infection. A recent study confirmed that the most common radiographic abnormality is a bronchial pattern, but an unstructured interstitial pattern can be present in many cats. More than half of the cats in that study had lung hyperinflation also. [2] Bronchiectasis can be identified in a smaller number of cats. Right middle lobar atelectasis can be seen, as can small nodules throughout the lung and represent mucous plugs with granuloma formation.

Severe inflammatory lower airway disease can lead to hyperinflation with a flattened diaphragm. The bronchial pattern can be mixed with small nodules due to mucous plugging and exudates.

Interstitial lung disease
Primary Neoplasia
Primary pulmonary neoplasia is relatively uncommon in cats and generally has a poor prognosis. Radiographically it is typically a solitary or multiple masses, or, a disseminated lung pattern or lobar consolidation that looks like pneumonia. Adenocarcinoma may be come cavitated. Bronchoalveolar cell carcinomas and squamous cell carcinoma are usually diffuse in the lung. Most pulmonary tumors are in the caudal lobes. Adenocarcinoma is reported as the predominant tumor type, but shares many features with less common tumor types. Prevalence of suspected intrapulmonary metastasis was higher than in previous radiographic studies of cats with lung tumors. [3]

Metastatic neoplasia
Metastatic neoplasia generally present as multifocal small round soft tissue pulmonary nodules. In cats, lung-digit syndrome is an unusual pattern of metastasis that is seen with various types of primary lung tumors, particularly bronchial and bronchioalveolar adenocarcinoma. Tumor metastases are found at atypical sites, notably the distal phalanges of the limbs; the weight bearing digits are most frequently affected, and multiple-digit and multiple-limb involvement is common.[4]

Pulmonary Fibrosis
Pulmonary fibrosis is a progressive fatal interstitial lung disease that is often idiopathic, occurs in multiple species, and may be caused by a number of inciting factors. A recent study of nine cats showed that all patients had a broad range of radiographic characteristics that included broncho-interstitial pattern, alveolar pattern, pulmonary masses, pulmonary bullae, pleural effusion, and cardiomegaly. [5] Cats in that study with echocardiographic studies had characteristics that included right ventricular dilation and hypertrophy and pulmonary arterial hypertension interpreted to be secondary to primary lung disease. Cats with pulmonary fibrosis have highly variable radiographic characteristics and that these characteristics may mimic other diseases such as asthma, pneumonia, pulmonary edema, or neoplasia. [5]

Vascular Disease
Heartworm disease can cause enlarged pulmonary arteries. However, the pulmonary findings may also be rather unremarkable in infected cats. An airway pattern is often present in most cases as well. Cardiac abnormalities are not typical.

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FIP Updates: Optimizing Treatment Now & Into the Future

Sally Coggins, BVSc (Hons), MANZCVS (Feline Medicine)

Background

Feline infectious peritonitis (FIP) is now considered a treatable disease, with disease remission and long-term survival repeatedly demonstrated following administration of new generation antiviral drugs, primarily the nucleoside analogue GS-441524.[1-6] Despite published evidence of the therapeutic power of GS-441524 since 2018, the main barrier to treatment globally has been the lack of registered veterinary products. One of the silver linings of the COVID-19 pandemic was that veterinarians in Australia, and subsequently other countries such as the United Kingdom and New Zealand, have been able to obtain legal compounded versions of GS-441524 and its prodrug remdesivir (GS-5734). Veterinarians in Australia now also have legal access to molnupiravir (EIDD-2801) and will soon have access to a compounded version of that drug's core nucleoside analogue, EIDD-1931. The repurposed antimalarial drug mefloquine is also sometimes utilized as an adjunct to these new generation antivirals. Overall, the survival rates achieved using various formulations of GS-441524, remdesivir or molnupiravir range from 77 to 96%.[2,4-7]

Dosage Regimens

GS-441524 and remdesivir

GS-441524 is the core nucleoside analogue. Compounded versions are typically formulated as oral 50 mg tablets, ¼ scored. Unregistered products are available as oral tablets and may also be available in parenteral formulations. The active ingredients (including GS-441524) are often not disclosed on the packaging of unregistered products and the precise amount of GS-441524 they contain is often unknown. Analysis of several unregistered products performed in Australia showed that the quantity of active ingredient may be higher or lower than the value provided by the manufacturer, and to the author's knowledge, analyses of batch-to-batch variations in unregistered products have not been performed. The use of unregistered products remains illegal in many parts of the world although they are often readily accessed by owners online, and such unlicensed products have saved the lives of thousands of cats with FIP.[4,8] Remdesivir is the nucleotide pro-drug of GS-441524. It is metabolized to GS-441524 *in vivo*.[9] Compounded remdesivir is supplied primarily as a parenteral formulation [100 mg/10 mL vials (10 mg/mL)], however, some countries, e.g. New Zealand, have access to oral compounded capsules. The human registered product Veklury® may be available to veterinarians in some parts of the world but the concentration [100 mg/20 mL (5 mg/mL)] is half that of veterinary compounded formulations, often making this volume prohibitive for repeated subcutaneous injection in cats.

When comparing the molecular weight of remdesivir (the prodrug) to GS-441524 (the core nucleoside), 10-15 mg/kg of remdesivir is equivalent to 4.8-7.25 mg/kg GS-441524. Pharmacokinetics of orally administered GS-441524 and remdesivir at 25 mg/kg in clinically healthy cats have recently been documented to achieve plasma levels greater than EC_{50} values for over 24 hours (Cook 2022). Of note, however, inter-cat variability was high and further studies are required to fully assess the bioavailability of oral GS-441524 and remdesivir in cats with FIP, as absorption may be impacted by disease state. It should be noted that lower dosages of oral GS-441524 have been regularly utilized with successful treatment outcomes. For treatment regimens in Australia and the UK, it has become common practice when transitioning from parenteral remdesivir to oral GS-441524, to utilize the same dose rate (e.g., If a cat commences IV remdesivir at 15mg/kg, they will be transitioned onto oral GS-441524 at 15mg/kg).

Recommended dosage regimens vary according to the presenting form of FIP, with it currently recommended that cats with effusive disease be treated with lower dose rates compared to non-effusive forms.

Table 1. Treatment protocols adapted from Coggins et al 2023 in submission

FIP presentation	**Induction dosage (First 3-5 doses)** Remdesivir slow IV* or SC	**Maintenance dosage (to complete 84-day treatment)** Remdesivir SC OR GS-441524 PO^
Effusive (no neurologic/ophthalmic involvement)	10-15 mg/kg q 24 h	10 mg/kg q 24 h
Non-effusive (no neurologic/ophthalmic involvement)	15 mg/kg q 24 h	10-15 mg/kg q 24 h
Ocular involvement	15 mg/kg q 24 h	12-15 mg/kg q 24 h
Neurologic involvement	20 mg/kg q 24 h	20 mg/kg SC or 20 mg/kg as divided dose PO (e.g., 10 mg/kg q 12 h PO)

*Slow IV – Give as CRI over 20-30 minutes, can be diluted with 0.9% saline
^PO – Round up to the nearest ¼ tablet. Administer to cat in fasted state with water bolus or one tablespoon of wet food, full meal 30 minutes later.

Whilst both remdesivir and GS-441524 appear to be very well tolerated in cats, the use of parenteral therapy during the initial treatment phase is hypothesized to achieve more rapid tissue concentrations of the active intracellular triphosphate, although tissue concentrations achieved have not been quantified in cats. Parenteral formulations also facilitate commencement of treatment in moribund cats where oral therapy would not be feasible. Oral therapy, however, often represents a more cost-effective approach for clients and negates adverse events such as the injection site discomfort that is relatively common with subcutaneous injections. It should be noted that many anecdotal reports exist of clinicians utilizing oral GS-441524 as a sole therapy, even with neurologic cases, with similar response rates to parenteral regimens. Published use of unregistered formulations containing GS-441524 also support oral therapy to be effective from commencement of treatment.[4,5]

EIDD-1931 and molnupiravir
EIDD-1931 is the core nucleoside of the prodrug molnupiravir. Molnupiravir is now a commonly utilized oral antiviral for humans suffering with COVID-19 and has become more readily accessible to veterinarians in Australia via prescription. Less is known about the utility of this drug for treatment of FIP, however information is being rapidly collected and use is gaining popularity as molnupiravir can often be sourced less expensively than GS-441524 or remdesivir.

In Australia, the dosage regimen utilized for molnupiravir is 10-15 mg/kg BID PO for 84 days (12 weeks),[10] which is in line with owner-reported dosage regimens for use of unregistered molnupiravir published by Roy *et al* 2022,[7] with average dosages of 12.8-14.7 mg/kg BID PO. Cats receiving unregistered EIDD 1931 received similar dosages to molnupiravir. In this study, 92% of cats remained in clinical remission at the time of publication. Adverse effects included folded ear tips, severe leukopenia, brittle whiskers, flaky skin, nausea/vomiting, anorexia and muscle wasting.

Mefloquine
Mefloquine is an antimalarial drug shown to have antiviral effects on feline coronavirus *in vitro*,[11] is metabolised effectively by the liver *in* vitro[12], and is well tolerated in clinically normal cats.[13] A dosage regimen of 10-12 mg/kg PO twice weekly with food is proposed. The author is aware of a case of definitively diagnosed non-effusive FIP achieving sustained remission (>3 years) following treatment with mefloquine combined with feline omega interferon. The author is also aware of many cases receiving co-administration of mefloquine alongside 1, 2 or 3 months of treatment with GS-441524 with mefloquine administration continued once the GS-441524 has ceased (often for 6-12 months). For cases where the full 84-day course of a nucleoside/nucleotide analogue is cost prohibitive, co-administration with mefloquine from the commencement of treatment may offer an alternative to achieving remission, or at least prolonging quality of life.

Expected Response to Treatment
Below is a table of common clinical abnormalities observed at time of FIP diagnosis with expected times by which these abnormalities should resolve if cats are responding favorably to treatment. Prolongation of such abnormalities should prompt clinicians to consider a dosage increase by 5 mg/kg per day. If dosage increases are required beyond week 10 of treatment, it is currently suggested that treatment should be extended on a two-weekly basis until normalization has occurred and been sustained for at least 2 weeks. It should be noted that these time frames relate to compounded GS-441524 / remdesivir. Preliminary information suggests that such time frames may also be appropriate for use with EIDD-1931 / molnupiravir.

Table 2. Average days to normalization of key abnormalities in cats with FIP receiving treatment with remdesivir, adapted from Coggins *et al* 2023 in submission.

Abnormality	**Expected time to resolution**
Pyrexia / inappetence	2-7 days
Effusions	1-2 weeks*
Leukogram abnormalities	2-3 weeks
Hyperbilirubinemia	2-3 weeks
Albumin:globulin > 0.6	6-10 weeks
Ophthalmic / neurologic signs	Improve by day 5, resolution within 2 weeks^
*Effusion resolution frequently coincides with a transient decrease in body weight, decrease in PCV and increase in globulin concentration. These seemingly negative changes are expected and do not warrant dosage increases so long as cats are improving clinically (resolution of pyrexia, return of normal appetite and behaviours). ^Exceptions may include spinal cord deficits, which may take longer to respond (or may be permanent).	

Key things to avoid when treating FIP with parenteral remdesivir or oral GS-441524

- **DO NOT** allow dosage to decrease below 10 mg/kg at any point (estimate up so that cats are always growing into the dose).
- **DO NOT** adjust the dosage downwards with body weight decreases, only upwards with weight gains.
- **DO NOT** cease treatment before 12 weeks, even if the cat has responded quickly to therapy. With time, and as more robust trials are performed, it may be acceptable to reduce treatment duration, however at this stage, completing the full 84-day course is still recommended.

MINIMUM RECOMMENDED MONITORING TIME POINTS

- Physical examination (body weight measurement) every 2 weeks, with monthly blood tests.
- Focus on clinical response in the first 6 weeks of treatment.
- Blood work testing (hematology and serum biochemistry profile) at 6-8 weeks and 10-12 weeks are particularly crucial.
- If dosage increase is required, recheck 1-2 weeks after the change to ensure response.
- If course extension is required, recheck fortnightly until remission is achieved.

Future Hurdles

It is an exciting time in feline medicine to finally be in a position to treat this historically fatal disease, however, our knowledge surrounding treatment optimization is still in its infancy, with significant further work needed to continue to optimise feline patient outcomes now and into the future.

Key areas requiring further research include further investigation into combination antiviral therapy; refinement of approach to initial stabilization of advanced cases (as mortality appears to be highest during the first few days of treatment); refinement of optimal treatment duration; refinement of definition of “remission” and “cure” states; long-term longitudinal monitoring to assess if cats that achieve a cure are susceptible to FIP in the future (and would this represent re-exposure or recurrence of latent infection); are FIP survivors at a higher risk of other disease conditions?; is antiviral resistance likely to be an emergent threat to effective treatment of this disease.

Conclusion

Nucleoside and nucleotide analogues as monotherapy or in combination with other agents are proving to be highly effective and well tolerated, inducing long-term survival in cats with FIP. This is a rapidly evolving space in feline medicine and further prospective randomized trials are needed for all current and future antivirals. Clinicians are urged to regularly review new literature as it emerges over coming years. Combination drug therapy and continued revision of dosage regimens may allow further improvements to survival rate and reductions to treatment duration.

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2023 Spring into Feline Medicine

THREE-DAY **VIRTUAL LIVE CE EVENT**

Sunday, April 30th | Wednesday, May 10th | Saturday, May 20th

ALL TIMES ARE EASTERN TIME ZONE

Sunday, April 30, 2023

TIME	SESSION TITLE	SPEAKER	SPONSOR/PARTNER
12:00 - 1:00 pm	The Cat is Losing Hair: It's Not Allergies & it's Not Dermatophytes, Now What?	Dr. Catherine Outerbridge	
1:15 - 2:30 pm	Feline Regional Dermatoses: Skin Diseases that Target the Dorsal Muzzle, Footpads, or Sometimes Both	Dr. Catherine Outerbridge	
2:45 - 3:45 pm	The Do's and Don't's of Trauma	Dr. Steven Berkowitz	
4:00 - 5:00 pm	Feline Respiratory Emergencies: "Stat: Why is My Cat Panting?!"	Dr. Steven Berkowitz	

Wednesday, May 10, 2023

TIME	SESSION TITLE	SPEAKER	SPONSOR/PARTNER
2:00 - 3:00 pm	A Bright Future for Painful Cats: New, Improved, & Emerging Options for Multimodal Management of Feline Osteoarthritis	Dr. Erin Dresner	
3:15 - 4:15 pm	Feline Neurology: Pearls for Your Practice	Dr. Joane Parent	
4:30 - 5:30 pm	Improving Interpretation of Pulmonary Patterns	Dr. Lorrie Gaschen	
5:45 - 7:00 pm	FIP Updates: Optimizing Treatment Now & Into the Future	Dr. Sally Jayne Coggins	

Saturday, May 20, 2023

TIME	SESSION TITLE	SPEAKER	SPONSOR/PARTNER
12:00 - 1:00 pm	Management of Oral & Dental Pain	Dr. Heidi Lobprise	IVAPM
1:15 - 2:30 pm	Feline Stomatitis	Dr. Heidi Lobprise	
2:45 - 3:45 pm	Anterior Uveitis: Don't Miss The Big Stuff	Dr. Jessica Meekins	Dechra
4:00 - 5:00 pm	The Crystalluria Dilemma: When Should I Care About Crystals?	Dr. Julie Byron	ROYAL CANIN

American Association of Feline Practitioners
2023 Spring into Feline Medicine ● April 30, May 10 & May 20

Management of Oral & Dental Pain

Heidi Lobprise, DVM, DAVDC

Introduction

Oral and dental diseases, as well as any surgical intervention, can cause discomfort and inflammation in the oral cavity. From periodontal disease and fractured teeth to tooth resorption and even chronic pain, resolution of these issues can improve the quality of life of our feline patients. Management of oral and dental disease, as well as a comprehensive, multi-modal analgesic protocol can keep our patients comfortable and return them to health and function through optimal healing.

Cats in Pain – are Stressed!

Cats are really good at hiding pain and discomfort, and if there are obvious signs, the pain is likely significant or has been going on for a while. Behavior changes with interaction, decreased grooming and even aggression may be present. They may paw at their mouth, to the level of self-trauma or jump back from the food bowl when trying to eat, even though hungry. The Feline Grimace Scale has given us some good tools to evaluate cat body/head language to better assess if there is discomfort. Newer tools such as thermal imaging (more useful with limb pain) and now sensors and monitors that can quantify both acute and chronic pain using a biosignal generated by the nervous system.

Pain and behavior go hand-in-hand; a painful pet will be stressed, anxious and fearful. Pre-visit steps may be needed, such as having owners use appropriate carriers and even consent behavior training, as well as pre-visit pharmaceutics and pheromones. Pre-operative pain medication should be started on all patients whenever possible. Once we have the patient in the examination room, concepts of “cat friendly interactions in practice” and “cat friendly tips for dental examinations” from guidelines provided by AAFP/ISFM can also be employed to minimize the stress. If the carrier’s top can be easily removed, we can allow the cat to stay in a safe place. If they’d like, allow them to explore the room during conversation with the cat caregiver. The concepts of using a considerate approach with gentle control should be utilized, but with a specific oral issue, the touch gradient may be adjusted. That is one time the more stressful portion of the exam (oral assessment) might be done earlier in the process. Examine the mouth from behind or from the side of the face to be less alarming to the cat. Gentle scratching of the ears and under the chin can facilitate a gentle lifting of the lips to assess the extent of plaque, calculus, and gingival inflammation in general. Remember some cats can have a large buildup of calculus on the maxillary fourth premolars with minimal attachment loss, but the ‘thumbnail flick’ to remove the calculus chunk does not constitute a dental cleaning! (And bilateral ‘flicks’ are seldom tolerated). If possible, try to visualize 307 and 407, the most common teeth impacted by odontoclastic tooth resorption. 4 If those teeth, or any others, demonstrate signs of a missing crown or portions of the crown resorbed with ingrowth or apparent covering of the crown with gingiva, then the entire mouth needs full evaluation with dental radiographs. If there are signs of periodontal disease or inflammation and ulceration, or there are any concerns for possible stomatitis, the last part of your oral exam should include trying to open the mouth to visualize the caudal aspect of the oral cavity. You usually don’t have to pull down on the mandible; just gently grasp the maxilla over the top of the head and rotate the head back. They will often open their mouth sufficiently, though briefly, for you to visualize that region. Be very careful with cats that are painful and minimize handling when you can.

Common Painful Conditions

Tooth Resorptions (TR) are commonly found in our feline patients. If these are discovered as odontoclastic/replacement resorption (Type 2) confined to the root region during dental radiographs, there is likely little discomfort experienced by that patient. We do know that once the lesion extends into the crown (or type 1 Inflammatory TR is present), that there is a pain response when these teeth are ‘touched’ even under general anesthesia. The crown will eventually snap off with enough resorption, but by extracting the tooth, or even just removing the crown portion, we can make our patients more comfortable. Stomatitis (Feline Chronic Gingivostomatitis – FCGS) is likely one of the most painful oral issues a cat can experience; further information in that lecture.

Traumatic injuries are certainly painful, from soft tissue damage to tooth fracture, jaw fractures and even TMJ injuries such as luxation. Pain management is critical in these patients along with general care that will include food intake assistance. Oral tumors that enlarge to the extent that teeth cause self-injury or those that have osseous expansion likely contribution to pain and discomfort, but cats often don’t exhibit outward signs until the disease is well advanced, so regular examination is critical.

Chronic pain may be more challenging to recognize and diagnosis a specific cause or process. Feline Oral Pain Syndrome (FOPS) is a unique issue that is primarily seen in Burmese cats but can be found in any breed. This neuropathic pain disorder is due to a sensitization of the trigeminal nerve. Triggers from dental origin (teething in kittens, periodontal disease, etc) to stress triggers can start these episodes of extreme discomfort for the patient. Other causes of chronic pain may be results of other neuropathies, chronic TMJ osteoarthritis and refractory stomatitis.

Managing Pain

While the awake cat oral examination will give you a reasonable indication of disease in most cats (not all!), we know a complete evaluation cannot be done without general anesthesia, so we need to properly examine/evaluate our patients for their general health and anesthetic risks. Depending on the life stage, appropriate blood work, urinalysis, physical exam with auscultation and palpation, and blood pressure can give us most of the information we need to prepare that patient for anesthesia. With few exceptions, most patients can easily handle our personalized (or 'pet-alized') pain and anesthetic protocols. If there is any indication of discomfort or presence of a painful condition, pre-operative analgesia medication is indicated. There may be some that need further evaluation or stabilization prior to anesthesia, such as if there are cardiac, renal or other conditions present. Because the chronic inflammation that is present with dental disease can impact overall health (more than just bacteremia), it is important to provide optimal care. It is rare that dental care cannot be provided for a patient, especially those senior patients that would benefit from this care. Excellent anesthetic guidelines for cats have been developed by AAFP (2018 AAFP Feline Anesthesia Guidelines).

General principles of analgesia and anesthetic protocols can be utilized for dental procedures. Pre-visit pharmaceuticals such as gabapentin (for anxiety) will not have a significant effect on the use of sedatives, pain medication and anesthetics, so they should be given if helpful for the patient. Pre-anesthetic protocols often involve the use of an opioid, benzodiazepine and alpha 2 agonist, and even maropitant as appropriate for each patient. Be familiar with the compounds you have available and be able to recognize any indications for decreasing doses (senior patients, systemic diseases) or by using reversal agents if any unwelcome side effects are noted. Peri-operative protocols with loco-regional blocks, constant rate infusions and post-operative medications, will help keeping our patients as comfortable as possible and get them back to full function as quickly as possible. CRIs can provide small amounts of appropriate agents such as Ketamine (blocks NDMA receptors) and opioids to help keep the patient as comfortable as possible, help prevent wind-up pain or sensitization and minimize general anesthetic needs.

Local and Regional Blocks

My local anesthetic of preference is bupivacaine, placed at least 5-10 minutes prior to the procedure, at a dose not to exceed 1mg/kg for cats. Mixing lidocaine with bupivacaine does not significantly speed of onset but can decrease the duration of analgesia. When available, a premix of bupivacaine 0.5% with 1:200,000 epinephrine can extend the time the duration of the block (6 to 8 hours) and provides some vasoconstriction. Adding in buprenorphine (1 part buprenorphine to 9 parts bupivacaine) can also potentiate the duration of analgesia – greater than 24 hours. Another option for a longer lasting block is to use Nocita® (bupivacaine liposome injectable solution), that can provide up to 72 hours of analgesia in the blocked area. While a dental block is not specified on this product label (peripheral nerve block), this author is comfortable with using this agent for dental blocks.

There are two main regional blocks used for cats – a caudal approach to the maxillary block and the mandibular or inferior alveolar block (bilaterally). Since the infraorbital canal in a cat is often very short, with the eye immediately caudal to it, a standard infraorbital block may not be as effective, or can potentially cause problems. A caudal subzygomatic approach uses palpation of the ventral aspect of the rostral zygomatic arch. Keeping the needle and syringe parallel to the palate and aimed in a direction to the opposite nostril, the needle is advanced under the zygomatic arch until it approaches the area of the pterygopalatine foramen at the distal aspect of the infraorbital canal. Since the innervation to the maxillary 4th premolar and molar comes off the maxillary nerve prior to entering the infraorbital canal, infiltration as the needle is retracted will impact those teeth.

The inferior alveolar block (caudal mandibular block) can be done externally through the skin or intraorally through the mucosa. It is important to place the appropriate amount of the agent (not too much) directly at the caudal opening of the mandibular canal on the lingual aspect of the mandible. Limiting placement of the anesthetic where the nerve enters the canal will deter the agent from infiltrating further medially which could affect the lingual nerve (a rare occurrence). At 1mg/kg with a 0.5% product, this is only 1 cc for an 11-pound, 5 kg cat, limiting the amount at each of the 4 block sites to 0.25ml. In very small cats, dilution may be needed to provide sufficient volume for multiple sites.

Post Operative
Post operative pain management options in cats continue to improve. Onsior® (robenacoxib) as an NSAID (injectable and tablet) is a good choice to help manage pain and inflammation. Off-label use of meloxicam products can also provide some comfort. The use of buprenorphine administered onto the mucosa 2-3 times daily can provide additional pain relief. To avoid having to administer medications orally (unless a feeding tube is placed), many practices can now use a transdermal application of buprenorphine that lasts up to 4 days (Zorbium™ - buprenorphine transdermal solution). “Physical” therapy may include the use of e-collars (tailored for cat use), cool compresses, and targeted pulsed electromagnetic field devices.

Managing Chronic Pain
Once pain goes beyond the acute, reactive, ‘helpful’ stage, managing patients with maladaptive or chronic pain can be quite challenging. Refractory stomatitis in that patient that has had full mouth extraction can be one of the most frustrating situations in practice. Occasionally, with the extractions and appropriate pain and inflammation management, that patient might look great at the 2 week recheck, but often there is some mild to moderate caudal mouth inflammation. Since this is an immune response, sometimes the inflammation will never go away completely, but we can help minimize it. A multimodal approach that hinges on individual response may include hypoallergenic diets, low dose doxycycline, gabapentin, esterified fatty acid application (1-TDC) and microlactin products. Some patients may require low dose corticosteroid medication on an as-needed basis if the discomfort is severe.
The chronic pain of FOPS has a unique approach to treatment: the use of phenobarbital is often the most effective in these patients, with effect on the trigeminal nerve. Certainly, treating any triggers such as dental issue or managing stress can be helpful as well. Some benefit from gabapentin as add-in therapy.

Other chronic pain such as arthritis of the TMJ due to previous trauma (as well as other O/A in cats) have been treated on a multi-modal level as well, with long-term use of NSAIDS (off-label protocols), gabapentin and amantadine. With the introduction of an anti-NGF monoclonal treatment (Solensia), specific reports of treating TMJ OA have not been mentioned, but would be a consideration.

Chronic pain can also benefit by adding in some of the ‘physical’ therapy or complementary medicine. The tPEMF loops have been used in many applications in human and veterinary medicine, including oral pain. Acupuncture, nutraceutical, and in some states, cannabinoid products can be trialed in an individual to see what works best for their conditions.

Summary
Cats can be victims of acute and chronic pain involving the oral cavity. Recognition of conditions and tailoring appropriate protocols for these patients can keep them comfortable, happy (depending on the cat…), eating well and interacting with their caregivers for an improved quality of life.

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Feline Stomatitis

Heidi Lobprise, DVM, DAVDC

Introduction

Cats display several unique conditions when it comes to the oral cavity, even though the basic concepts of periodontal disease apply. Stomatitis can be a frustrating syndrome, and while conservative and medical choices may help patients in the early stages of the disease, often caudal mouth extractions become necessary eventually.

Feline Stomatitis

By definition – stomatitis means the inflammation of the mucous lining of any of the structures in the mouth; in clinical use, the term should be reserved to describe wide-spread oral inflammation (beyond gingivitis and periodontitis) that may also extend into submucosal tissues (e.g., marked caudal mucositis extending into submucosal tissues may be termed caudal stomatitis).

Inflammation limited to the gingiva (gingivitis) may be the only indication of early stomatitis, but when inflammation extends past the mucogingival line into the alveolar mucosa and even into the vestibular space, this alveolar mucositis generally signifies a more advanced process. While inflammation in the oral cavity can involve any group of tissues, from buccal mucositis to glossitis and palatitis, one of the most important regions to inspect is the mucosa of the caudal oral cavity. This region, bordered medially by the palatoglossal folds and the fauces, dorsally by the hard and soft palate and rostrally by alveolar and buccal mucosa, is often the site of significant to extreme ulceration and proliferation of tissues.

In a consensus statement from the AVDC and the European Veterinary Dental College, stomatitis can be divided into two types: Type 1 – cases with alveolar and labial/buccal mucositis/stomatitis only, or Type 2 – cases with caudal mucositis/stomatitis, with or without alveolar and labial/buccal mucositis/stomatitis. Identification of caudal mouth involvement is important, as these are the case that are generally most difficult to manage.

Extensive ulcerative and proliferative gingivitis and stomatitis with signs of excessive salivation, halitosis, decreased appetite and weight loss are often accompanied by histological presence of lymphocytes and plasma cells, often with a polyclonal hypergammaglobulinemia. While the distinct etiology is not defined, there are certainly components of bacteria, virus and environmental components all interacting with an over-responsive host immune system that contribute to a wide range of symptoms. Studies have shown a predominance of *Pastuerella multocida,spp multocida* and question now are being raised about potential fungal input. The likely dysbiosis of the mucosal microbiota can modulate host inflammatory response, which is a distinct issue in FCGS. The immune system in FCGS changes from a homeostatic defense to an up-regulated response. The oral mucosal tissue have high infiltration of B cells (but less in the circulation) and T cells (CD4+ and CD8+), as well as cells positive for an IL2 receptor (lymphocyte activation) and regulatory T cells. Patients also had high circulating CD8+ (cytotoxic) memory cells but a decrease in central memory cells, suggesting that there is a cytotoxic cell-mediated immune response to antigenic stimulation (viral). Genetic expression in affected cells was also altered from healthy mucosa, with enrichment for T-cell signalling, receptor interactions and cell-mediated toxicity.ref

With the immune-mediated basis, we can broadly consider an ‘antigenic’ model, though full avoidance of any allergens is unlikely. The immune response is also impacted by an infectious model, as some of the responses tie in changes in microbiota, involve intracellular viral load and possibly even fungal issues. Similarities in CD8+ populations in people with oral SCC also lead to questions about possible associations there. Many questions exist, from actually starts the inflammatory process and what input continue the inflammation and how do variable immune responses impact outcome.

FCGS Management

One thing we can do is try to somewhat standardize the evaluation of the extent of the disease, and the Stomatitis Disease Activity Index by Anderson helps with that. Measuring inflammation prior to any therapy and comparing to response can help us determine if a treatment is effective, at least in part. This SDAI information will be combined with a complete history of signs, previous therapy and response. At times, antibiotics and corticosteroids can make a less severe patient more comfortable, but client education is critical to avoid relying on these temporary measures. Especially in ‘early cases’, all of these patients should always be treated with a complete dental prophylaxis (with extractions as needed) and associated home care (as much as the patient will allow). If they respond well to this “Phase 1” approach, then focal periodontal disease or juvenile gingivitis may have been more likely. With more extensive inflammation and ulceration, particularly in the caudal mouth, true stomatitis may be present. We must be

careful to differentiate other diseases, from eosinophilic or pyogenic granulomas, as well as other ulcerations due to disease or even tumors. Acute calici virus can result in oral ulcerations, and research points to at least an association of this virus to FCGS, but it is more complicated than that.

Once caudal mouth inflammation is present (and sometimes with just alveolar and mucosal inflammation), therapy will often consist of extensive extractions. Previous data has shown that caudal mouth extractions (CME - premolars and molars) had similar results to full mouth extractions (FME), but each case is unique. There are several considerations to experience the best outcomes with FCGS extractions. Of course, full pain management is essential, from pre-operative protocols to effective blocks. Radiographs are needed to alert you to those teeth that may already have inflammatory resorption with fragile roots, as ALL root structure must be removed in these cases. Smaller, more delicate instruments, from 699 crosscut fissure cutting burs to section the teeth to small periosteal and dental elevators are key for optimal surgery. Since the gingiva is often inflamed and friable, there should be sufficient elevation and release of broad-based flaps into regions with soft tissue that will support sutures, including the lingual and palatal mucosa. After careful elevation of all tooth structure, alveoloplasty is another important step with these extractions. Any larger areas of rough bone can be removed with a carbide bur, but the edges (and alveoli) should be further smoothed with diamond burs. All inflamed tissue should be removed. My preference for closure is using 5-0 monofilament suture on a tapered (or cutting taper) needle, placing cruciate sutures with the knots buried from caudal to rostral. This minimizes any knots that can collect debris and cause irritation. Placement of feeding tubes can enhance post-operative nutrition and decrease the presence of food particles at the healing tissues.

Refractory cases

Seldom are the oral tissues going to be completely ‘calm’ at a 2 week recheck, so regular follow-up visits are important. If the canines were not extracted, and inflammation persists or worsens, or if ulceration is already significant at the canine teeth, they may need to be extracted as well, but they should be preserved until necessary. Even with all the teeth removed, there are still plenty of bacteria in the oral cavity, from gingival sites to the tongue. It is impossible to get the oral cavity completely antigen-free, but by minimizing the surfaces plaque can adhere to, many patients show significant improvement. Those with advanced proliferative lesions in the caudal mouth and pharynx have a much more guarded prognosis and will often need a combination of treatments just to get by. The list of possible therapies is as long as the list of questions we still have about FCGS. When we get better answers as to the ‘cause’ and etiologic progression, we will be able to have more distinct therapeutic options. For now, providing for the best comfort of our patients may include a wide range of choices: corticosteroids (as needed basis), cyclosporin, interferon, anti-inflammatory medications, low dose doxycycline, esterified fatty acids, tPEMF, laser therapy, etc.

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Anterior Uveitis: Don't Miss The Big Stuff

Jessica Meekins, DVM, MS, DACVO

Introduction

Uveitis, or intraocular inflammation, may occur as a manifestation of systemic disease or as a problem limited to the eye. The uveal tract is the middle or vascular tunic of the eye, and it is divided into the anterior (i.e., iris and ciliary body) and the posterior (i.e., choroid) components. The uveal tract allows for a direct connection between the eyes and the body. Certain disease processes confined to the eye (i.e., idiopathic/immune mediated) can lead to uveitis, but primary ocular uveitis is generally considered a diagnosis of exclusion after ruling out potential systemic diseases. The clinician must always consider that uveitis could be an ocular manifestation of a more widespread problem.

Clinical Presentation

Signalment and History

Uveitis can affect cats of any age or breed, however certain age groups (kitten vs. adult cat) or specific risk factors (indoor vs. outdoor) may influence the initial clinical suspicion of uveitis etiology. Because the clinical signs of uveitis can be subtle, the history may vary widely from a sudden onset change in appearance of the eye(s) to a more slowly progressive change occurring over several weeks. Vision status as perceived by the owner can be quite variable, and is dependent on the location and severity of inflammation within the eye(s). Cats are very adept at adjusting to even advanced vision loss, such that some owners are unaware of marked vision impairment until it is brought to their attention based on the results of an ophthalmic examination.

The Ophthalmic Examination

Most veterinary practices are equipped with the basic tools for ophthalmic examination. These include a direct ophthalmoscope, a Finoff transilluminator or penlight, and fluorescein stain strips. Digital tonometry to measure intraocular pressure is also becoming more readily available in general practice. Each ophthalmic examination should start with a basic neuro-ophthalmic assessment, so that the examiner can confirm vision status and generally identify clues regarding the location of inflammation within the eye. Menace response, palpebral reflex, dazzle reflex, and pupillary light reflexes are important aspects of the initial assessment.

Aqueous flare, or protein within the anterior chamber fluid, is considered the pathognomonic sign of anterior uveitis. Protein leaks into the aqueous humor as a result of inflammation of the anterior uveal blood vessels. Using the direct ophthalmoscope, the examiner aims the small slit beam of light into the eye and evaluates the light striking the eye from a 45° angle. In a normal eye, the light strikes the cornea and the surface of the iris and lens, and the clear space in between these light columns represents the anterior chamber. In an eye with aqueous flare, that clear space is instead occupied by a diffuse, homogenous haziness. This is sometimes described as 'headlights in fog' and represents the Tyndall effect, whereby light is scattered by particles (i.e., protein) within a fine suspension (i.e., the aqueous humor).

Two other important signs of anterior uveitis are miosis (a small pupil) and hypotony (low intraocular pressure). The pupil constricts with uveitis due to the effects of inflammatory mediators on the iris tissue, while the intraocular pressure is low due to decreased production of aqueous humor by the ciliary body; the ciliary body epithelium experiences dysfunction in an inflammatory environment.

There are several other clinical signs of anterior uveitis, including keratic precipitates (i.e., clumps of white blood cells on the corneal endothelium) and the accumulation of other 'materials' in the anterior chamber (e.g., hypopyon, hyphema, fibrin). Together, these signs are the most important clues that lead the clinician to a preliminary diagnosis of anterior uveitis. While all signs are not necessarily present simultaneously, any combination of one or more signs is usually enough to make a diagnosis.

Posterior uveitis can be more difficult to recognize, depending on the degree of anterior uveitis that may be obscuring physical examination of the anterior portion of the eye and on the examiner's experience with performing and interpreting fundic examination. Significant manifestations of posterior uveitis include retinal detachment, retinal hemorrhage, and inflammatory infiltrates within or below the retina resulting in altered tapetal reflectivity. Depending on the severity of posterior uveitis, there may be signs of its presence during the initial neuro-ophthalmic assessment; for instance, an eye with a retinal detachment or significant posterior inflammatory infiltrates should have a diminished or absent menace response and abnormalities in the resting pupil size and pupillary light reflexes.

However, neuro-ophthalmology is a complicated topic, and partial retinal detachments or focal areas affected by inflammatory infiltrates may result in no signs or very subtle signs of neuro-ophthalmic deficits.

Whenever possible, the pupils of a cat with uveitis should be dilated to screen for involvement of the posterior segment. This will allow the examiner to identify abnormalities at the periphery of the ocular fundus that may be missed during a non-dilated exam. The eye is screened for signs of retinal detachment, hemorrhage, or altered reflectivity of the tapetum. Hypo-reflectivity occurs when material (e.g., fluid, cells, organisms) leaks out of the choroidal blood vessels and collects in the subretinal space. Remember that the tapetum is located within the choroid, so any material that leaks from the choroid will settle in between the retina and the tapetum, effectively dampening the tapetal 'shine' as viewed by the examiner.

While signs of anterior uveitis are arguably easier to recognize than posterior uveitis, fundic examination is an important part of a complete ophthalmic examination. Certain etiologies of uveitis preferentially affect different areas of the uveal tract and result in somewhat classic or characteristic lesions, so it is important to fully evaluate the eyes of each cat to screen for involvement of all aspects of the uveal tract (i.e., panuveitis).

Etiology

The uveal tract is the location of the blood-ocular barrier, with the blood-aqueous barrier anteriorly and the blood-retinal barrier posteriorly. The blood-aqueous barrier is formed by the endothelium of the iris blood vessels and the non-pigmented epithelium of the ciliary body, while the blood-retinal barrier is formed by the endothelium of the retinal blood vessels and the retinal pigment epithelium.[1] This barrier effectively protects the delicate tissues of the eye from the rest of the body, separating the intraocular structures from the blood entering the eye and systemic circulation. This protective barrier fails when inflammation leads to breakdown of its various components, resulting in exposure of the eye to elements from the body.

Infectious Organisms

There are a wide variety of infectious agents that may result in uveitis as an ocular manifestation of systemic disease.[2,3] The geographic specificity of select agents should be considered when building a list of potential infectious causes of feline uveitis. Viral (e.g., FIV,[4] FeLV,[5] FIP[5]), bacterial (e.g., bartonellosis,[6] leptospirosis), rickettsial (e.g., Ehrlichiosis, Lyme disease, Rocky Mountain Spotted Fever), protozoal (e.g., toxoplasmosis,[7] cytauxzoonosis[8]) and fungal (e.g., histoplasmosis, blastomycosis, cryptococcosis, coccioidomycosis) are some of the infectious agents that may occupy the differential list. In general, younger cats and those that have outdoor access are considered at an increased risk of infectious uveitis, though a fair number of cats housed exclusively indoors have been diagnosed with systemic infections causing uveitis.

Neoplasia

Ocular neoplasia is divided into primary and metastatic. While primary intraocular tumors (i.e., diffuse iris melanoma) may cause uveitis later in the course of disease, metastasis is considered the more common manifestation of neoplastic uveitis. The most common metastatic tumor to the feline eye is lymphoma,[5] though any distant site tumor may spread to the eye.[9]

Idiopathic/Immune mediated

A large proportion of adult cats, particularly indoor-only cats, are diagnosed with idiopathic lymphocytic-plasmacytic uveitis, which is essentially a form of immune-mediated uveitis.[10] The trigger for this attack of the host immune system against the eye is not well-understood, and idiopathic uveitis must be a *diagnosis of exclusion* after eliminating any potential systemic diseases that could be manifesting in the eye.

Concurrent Conditions

Non-ocular conditions that exist concurrently with uveitis are often referable to the underlying etiology and how it affects other organ systems. The most important ocular sequela of uveitis is secondary glaucoma,[11] which can be blinding and painful. Uveitis leads to glaucoma via several mechanisms. Acutely, the material that leaks into the anterior chamber (e.g., fibrin, cells) can physically block the fluid drainage angle located at the base of the cornea and iris (i.e., iridocorneal angle). Chronically, the outflow of fluid can be obstructed at the level of the pupil (i.e., posterior synechiae) or at the angle opening (i.e., pre-iridal fibrovascular membrane [PIFM] or peripheral anterior synechiae).[12] Acutely, the changes that result in an inappropriately high pressure – remember, the pressure inside the eye should be low in an inflammatory environment – are reversible; chronically, the changes are irreversible and secondary glaucoma will be managed long term.

Pupil block occurs when posterior synechiae, or adhesions between the pupil margin and the lens, develop circumferentially for 360°. This effectively prevents fluid being produced at the ciliary body from flowing through the pupil, which is necessary in order for it to be drained from the eye at the level of the iridocorneal angle. In an

inflammatory environment, the iris tissue becomes ‘sticky’ and prone to attaching to any closely located structure(s). The pupil also typically becomes miotic, which increases the proximity of the iris tissue to the lens. It is then easy for the iris at the pupil margin to come into contact with surface of the lens, forming adhesions that, if extensive, block fluid flow through the pupil.

The angle opening can be affected in two distinct ways. First, the cytokines and other inflammatory mediators that circulate inside the eye in an inflammatory environment promote the formation of a fibrovascular membrane on the iris surface (i.e., PIFM). This PIFM carpets the iris surface and ultimately grows across the angle opening, establishing a barrier to normal fluid outflow. Clinically, a PIFM can be identified during ophthalmic examination by observing a fine network of blood vessels on the iris surface and/or by noting a color change to the iris. The color change is most obvious in cats with blue irises.

The second mechanism of angle blockage occurs when the base of the iris swells and becomes displaced anteriorly, allowing the tissue to contact the peripheral cornea at the level of the angle opening. As was described regarding the pathophysiology of posterior synechiae development, similarly the tissue at the iris base is sticky and prone to attaching to neighboring structures. In this example, the iris tissue sticks permanently to the peripheral cornea and leads to an outflow obstruction.

Differential Diagnosis

The clinical signs of uveitis are distinct. No other ophthalmic disease results in aqueous flare or hypotony, and the only other disease that may cause a miotic pupil is Horner’s syndrome, a condition resulting from disruption of the sympathetic innervation to the eye and associated structures. Though there may be some overlap of clinical signs caused by uveitis and Horner’s syndrome, anterior chamber infiltrates (e.g., flare, cells, fibrin) should be absent and the intraocular pressure should be normal in an eye with miosis due to sympathetic denervation to the eye. This makes the differentiation between an inflammatory and a neurologic ophthalmic condition fairly straightforward.

Diagnostic Evaluation

A detailed history and thorough physical examination should be performed in any cat diagnosed with uveitis. The history should include information on environment (indoor/outdoor), vaccination and preventative status, and any travel history. The general physical examination is aimed at identifying any non-ocular abnormalities that may help narrow the list of potential uveitis etiologies. If any abnormalities are encountered, diagnostics can be targeted at further characterizing these findings. It is prudent to start with a minimum database (CBC, serum biochemical profile, urinalysis) in order to identify any non-specific changes that may accompany certain etiologies, as well as to provide baseline information on patient status prior to implementing treatment. Thoracic and abdominal imaging may be pursued, depending on physical examination findings. Selected infectious disease screening tests may also be performed; at minimum, an FIV/FeLV combo test should be done, even if the cat was previously tested and negative. This is particularly important if the cat has outdoor access and increased risk of exposure to these highly transmissible retroviruses due to contact with other, potentially infected cats. Other testing can then be prioritized based on the clinician’s index of suspicion for specific etiologies; a number of academic and private sector diagnostic laboratories offer a broad array of antigen testing, serology, and molecular diagnostics.

Management

Controlling inflammation, alleviating pain, and minimizing the development of sequelae are the goals of uveitis therapy. Specific therapy, such as antimicrobials for infectious uveitis or chemotherapy drugs for neoplastic (metastatic) uveitis, should be implemented in addition to symptomatic therapy when a specific cause is identified during diagnostic workup.

Anti-inflammatory therapy

Route of administration and type of drug are two important considerations when building the treatment plan for feline uveitis. Anterior uveitis is generally easier to treat when compared to posterior uveitis; topical ophthalmic preparations (drops, gels, ointments) are only able to penetrate to the level of the lens, so this route of treatment is ideal for anterior uveitis. Posterior uveitis, on the other hand, requires systemic therapy in order for the drug to reach its target within the back of the eye at the choroid. Options for systemic anti-inflammatory therapy are limited in cats, largely due to the decreased capacity for hepatic glucaronidation in the species.

Non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids are used to control inflammation in cats with uveitis.[13-15] Topical NSAIDs commonly used by the author include flurbiprofen, diclofenac, and ketorolac. These drugs are most appropriately used in cats with an ocular comorbidity that precludes the use of topical steroids (i.e., a corneal ulcer or increased risk of reactivation of latent herpesvirus), or they can be used in combination with topical steroids for an enhanced anti-inflammatory effect in more severe or medically refractory cases of uveitis. In general, steroids are preferred for their increased potency in more rapidly and effectively controlling active uveitis. When signs

of active anterior uveitis are identified on ophthalmic examination, topical steroids (NeoPolyDex or 1% prednisolone acetate) should be prescribed unless there is a specific contraindication to their use. NeoPolyBac with Hydrocortisone is inappropriate for treatment of anterior uveitis because hydrocortisone does not penetrate inside the eye.[13,14] The frequency of topical anti-inflammatory therapy is dictated by the severity of the inflammation, generally two to four times per day.

Because of the limited systemic absorption of topically applied medications, topical NSAIDs and steroids can be used together and topical steroids can be used even if there is concern for infectious uveitis. It is also generally safe to prescribe a topical NSAID and a systemic steroid, or a topical steroid and a systemic NSAID. Anterior uveitis should be treated with topical +/- systemic anti-inflammatory therapy, but posterior uveitis must be treated with systemic therapy in order to reach the affected tissue within the back of the eye. In the United States, systemic NSAID options are limited to 1) meloxicam as a single parenteral or oral dose, and 2) robenacoxib (Onsior®), which is labeled for once per day for up to 3 consecutive days, parenteral or oral use. In a study evaluating the ability of robenacoxib to inhibit experimentally induced anterior uveitis, there was no difference in uveitis scores for treated vs. control cats.[16] However, it remains to be determined if robenacoxib may be beneficial in cats with spontaneous, naturally occurring uveitis.

The other option for systemic anti-inflammatory therapy in cats is corticosteroids. It is fairly common to prescribe an anti-inflammatory dose of oral prednisolone in cats with posterior uveitis, especially when an infectious etiology is deemed unlikely.

Mydriatic (anticholinergic) therapy
Atropine is a useful addition to the medical therapy plan in feline uveitis.[17] Spasms of the ciliary body muscle are responsible for the pain that accompanies uveitis, and atropine alleviates pain by temporarily paralyzing that robust intraocular muscle. Atropine treatment also serves an important role in minimizing sequelae of uveitis, by dilating the pupil to decrease the risk of posterior synechiae formation and by stabilizing the blood-aqueous barrier.[17,18] In a non-inflamed eye, the effects of atropine can be quite long; depending on the species, the pupil may remain dilated for days to a week or more. While some clinicians advocate using pupil dilation as the determining factor for dosing frequency with atropine, it is important to note that the mydriatic effects have a longer duration than the cycloplegic effects. This means that consistent treatment is necessary for the duration of active uveitis signs in order to achieve all the benefits of atropine therapy. From a practical perspective, it is also important to consider that atropine has a bitter taste; some clinicians believe that ointment should be used instead of solution in cats in an effort to mitigate the hypersalivation that can accompany a dose of topical ophthalmic atropine. However, some cats are so sensitive to the bitter taste of atropine that hypersalivation occurs no matter what formulation is used.

In the author's experience, the majority of adult cats with anterior uveitis are ultimately diagnosed with idiopathic uveitis, while cats with posterior uveitis are often experiencing an ocular manifestation of systemic disease (e.g., infection, neoplasia, etc.). Any cat, regardless of age or exposure risk, may develop uveitis due to systemic disease, thus idiopathic uveitis must remain a diagnosis of exclusion after eliminating specific causes with a targeted diagnostic workup.

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American Association of Feline Practitioners
2023 Spring into Feline Medicine ● April 30, May 10 & May 20

The Crystalluria Dilemma: When Should I Care About Crystals?

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Introduction

For years I have had calls and emails from veterinarians, former students, clients, and colleagues about the abnormal urinalysis results. As the primary urologist in the practices I have joined, I am usually the one to field these. One of the most common questions I get is why a particular cat still has crystals (of any type) in its urine, especially after the diet has been changed to one that 'prevents' those crystals, or when the pH of the urine does not match up with the type of crystal present. For years we were taught to 'manage' crystalluria to prevent uroliths, decrease signs of FIC, and reduce lower urinary tract obstruction in cats so it is understandable that this is a frustrating topic for veterinarians. However, in the end, the level of concern we have is not warranted most of the time. One of the most important things I teach my students is that CRYSTALS ARE NOT (usually) DISEASE.

Physics of solutions

Remember dissolving sugar or salt in water and learning that the warmer the solution is the more you can dissolve in it? Then we would keep the beaker on the heat and let the water evaporate until the solution was supersaturated. By disturbing the solution or cooling it down we could get it to the point that crystallized material would come out of solution, hopefully if it was sugar, onto a string you had placed in the beaker for your own rock candy. Similar principles apply in our patients.

Cats have some of the best urine concentrating ability of domesticated species. They have an enormous range and even cats that have chronic kidney disease can often have urine specific gravities of > 1.025. Thus, it is not uncommon to find very concentrated urine in a patient at an exam. The highly concentrated urine has many solutes dissolved in it and often it is concentrated enough that there is some precipitation at the microscopic level. This is where the crystals we see in our patients are from most of the time. Dilute urine rarely has many crystal in it because they are staying in solution. This of course does not always apply to patients with underlying conditions that subject them to stone formation, but for most cats, the presence of struvite or calcium oxalate crystals (or both) is a benign finding.

Crystals vs. Uroliths

- Crystals form in concentrated urine, often regardless of the pH.
- They are not necessarily pathogenic
- They do not necessarily show up in cats with uroliths
- They do not predict that cat will be a stone former
- They can develop *ex vivo* in refrigerated or evaporated samples
- Cystine and urate crystals may require further evaluation

- Uroliths are pathogenic
- They form in concentrated urine
- Some cats are chronic stone formers
- Uroliths may require dietary management to prevent occurrence, *but not always*
- They may be related to a genetic or other underlying problem

When do I worry about crystals?

Struvite and calcium oxalate crystals are the most common ones we expect to see in cat urine. These are not usually a concern in most cats, especially those with no history of lower urinary tract signs. These are commonly seen in urine that is concentrated about 1.040, or even less. The presence of these crystals does not imply that uroliths are present, or that there is an increased risk of urolithiasis in the majority of cats. In fact, often there are few crystals in the urine of cats with uroliths because they precipitate onto the stone itself, not freely in the urine.

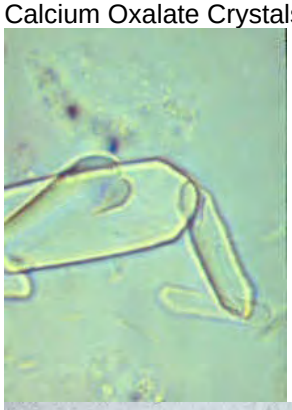
Crystals mean something different in cats that have a history of urolithiasis or males with history of urethral obstruction. In those cats, we are frequently trying to reduce the urine specific gravity and *under-saturate* the urine with calculogenic substances, and in the case of struvite uroliths, we are trying to maintain a more acidic pH. The presence of struvite or calcium oxalate crystals (depending on the type of urolith previously formed) indicates that we are not achieving our goals. They are the 'canary in the coal mine' so to speak. Crystals should not form in properly under-saturated urine.

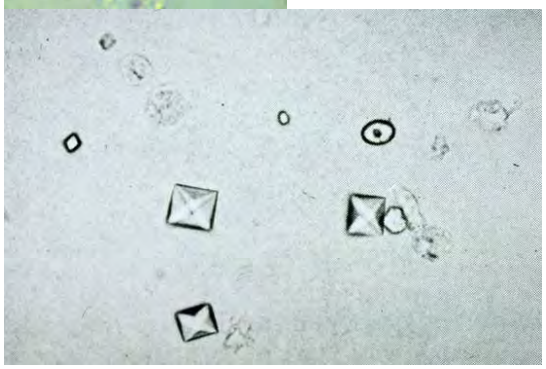
Urate and cystine crystalluria is rare in cats. Some cats are urate stone formers without any of the underlying hepatic or other metabolic abnormalities that cause urate urolithiasis in other species. These cats often have urate crystals in their urine before they form uroliths. Some cats with urate crystalluria may never form urate uroliths. However, due to the increased risk of developing uroliths, these cats should probably be placed on a low purine diet, often vegetarian, with a soy-based protein component to assure adequate protein levels. Allopurinol has also been used in these cats. Cystine crystals are also of concern, since they signal a high risk of development of cystine urolithiasis. Although rare in the cat, guidelines for treatment include increasing urine pH to improve solubility. As with all cats with increased urolithiasis risk, dilution of the urine to < 1.030 is highly recommended.

Finally, I do not ignore crystalluria in cats with lower urinary tract signs such as straining, periuria or hematuria. It is an indication that I should evaluate the lower urinary tract and verify there are no uroliths. Contrary to 'popular belief' the 'sharp' nature of crystals has not been shown to do any damage to the urothelium at the microscopic level. However, uroliths of any type can cause such injury.

Below are examples of the appearance of the most common types of crystals seen on feline urine sediments.

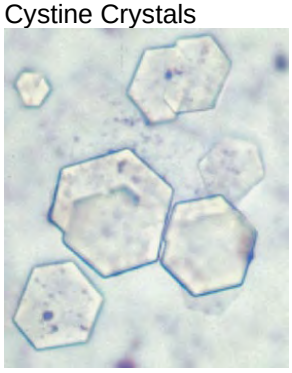
Calcium Oxalate Crystals



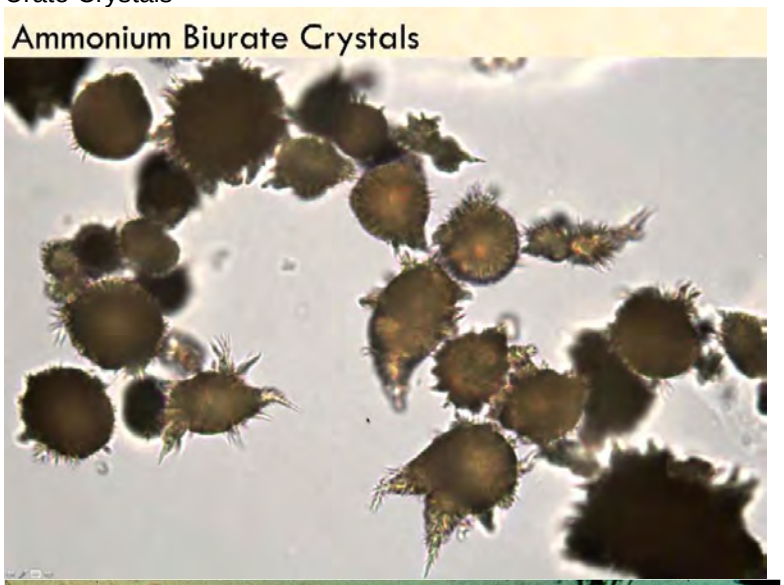


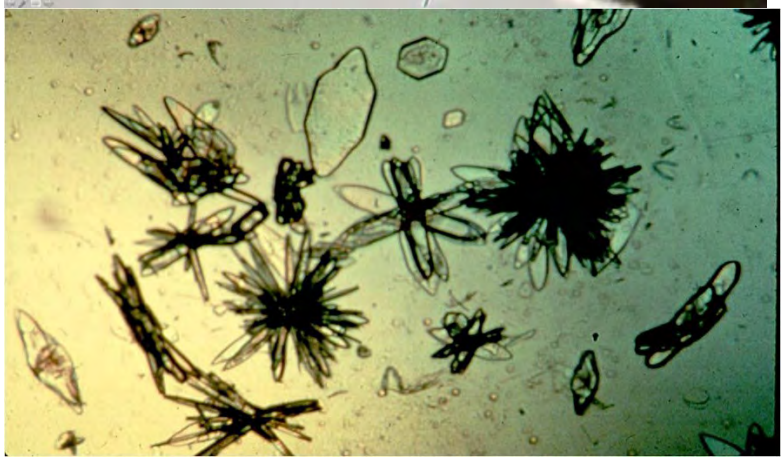
Struvite Crystals

Cystine Crystals



Urate Crystals





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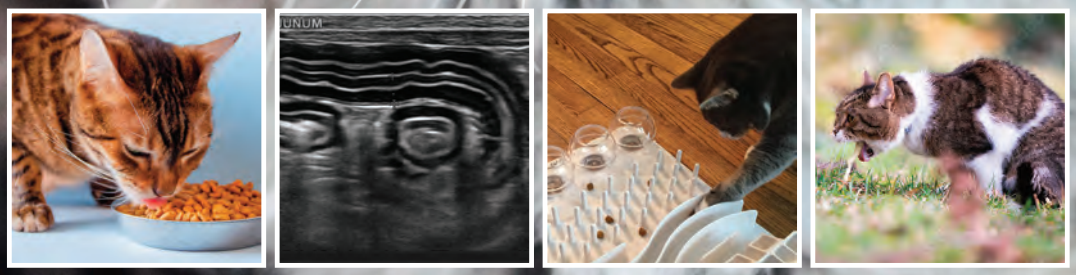

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