

AMERICAN ASSOCIATION OF FELINE PRACTITIONERS

Spring into Feline Medicine



Sunday, April 18th | Wednesday, April 28th | Saturday, May 8th

THREE-DAY VIRTUAL LIVE CE EVENT



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Top Tips for Management of Stress-associated Conditions in Cats

Christopher Pachel, DVM, DACVB, CABC

Feline Behavior: More Than Just a Naughty Cat

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Cutting Edge Updates on Chronic Kidney Disease: Understanding Dietary Phosphorus & Renal Health

Jonathan Elliott, MA, VetMB, PhD, DECVPT, MRCVS, FHEA

Cutting Edge Updates on Chronic Kidney Disease: Bone Mineral Disturbances – What Do We Know & Why Does it Matter?

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THREE-DAY **VIRTUAL LIVE CE EVENT**

Sunday, April 18th | Wednesday, April 28th | Saturday, May 8th

ALL TIMES ARE EASTERN TIME ZONE

Sunday, April 18, 2021

TIME	SESSION TITLE	SPEAKER	SPONSOR
12:00 - 1:20 pm	Top Tips for Management of Stress-associated Conditions in Cats	Dr. Christopher Pachel	
1:40 - 2:40 pm	Feline Behavior: More Than Just a Naughty Cat	Dr. Christopher Pachel	
2:50 - 3:50 pm	Feline Hypersensitivity Dermatitis: Understanding Cause & Therapy	Dr. Michael A. Rossi	
4:00 - 5:00 pm	Role of Probiotics in the Management of Diarrhea in Cats	Dr. Michael Lappin	

Wednesday, April 28, 2021

TIME	SESSION TITLE	SPEAKER	SPONSOR
12:00 - 1:20 pm	Peak Cat Care: Getting the Most from your Feline Exam	Dr. Elizabeth Colleran & Dr. Margaret Gruen	
1:40 - 2:40 pm	Cutting Edge Updates on Chronic Kidney Disease: Understanding Dietary Phosphorus & Renal Health	Dr. Jonathan Elliott	
2:50 - 3:50 pm	Cutting Edge Updates on Chronic Kidney Disease: Bone Mineral Disturbances – What Do We Know & Why Does it Matter?	Dr. Jonathan Elliott	
4:00 - 5:00 pm	Learning the Ins & Outs of Taking Feline Blood Pressure Without Elevating Yours	Ms. Ellen Carozza & Dr. Kelly St. Denis	

Saturday, May 8, 2021

TIME	SESSION TITLE	SPEAKER	SPONSOR
12:00 - 1:20 pm	Keeping Felines Feisty Despite Frailty	Dr. Shelia Robertson & Dr. Bonnie Wright	
1:40 - 2:40 pm	Nutritional Myths: Cat Owner Questions & Concerns	Dr. Julie Churchill	
2:50 - 3:50 pm	Complicated Endocrine Cases	Dr. Cynthia Ward	
4:00 - 5:00 pm	Secrets to Managing Today's Diabetic	Dr. Cynthia Ward	

Top Tips for Management of Stress-associated Conditions in Cats

Christopher Pachel, DVM, DACVB, CABC

Every intervention plan for addressing feline stress first must include the recognition of the stress itself, either by the pet owner or the caregiver who is making recommendations, or both. This awareness typically comes from noticing body language changes, shifts in social interaction patterns or daily activity, or perhaps identifying changes in the physical health of the animal that might have an underlying stress component (upper respiratory infection, colitis or constipation, inflammation in the lower urinary tract, increase in pruritis, etc.). Once both the caregiver and the veterinary team are on the same page regarding the need for intervention or support, what comes next?

Overview of Intervention Options

A comprehensive approach to behavioral management and treatment typically consists of a three-pronged strategy: behavior modification, environmental management, and “medication” (which may include nutritional support, supplements, pheromones, pharmaceuticals, etc.). Not every plan encompasses all three prongs, but all are typically considered for each patient to determine which combination is the most appropriate for a specific pet and owner's needs.

Hierarchy of Behavior Change

Another way to look at the available interventions is using the Hierarchy of Behavior-Change Procedures that outlines a LIMA (least intrusive, minimally aversive) approach to this treatment and management process. This hierarchy (<https://m.iaabc.org/about/lima/hierarchy/>) starts with an evaluation of the animal's health, nutritional, and physical factors by a veterinarian to ensure the baseline status of the animal. This is followed by an assessment of the physical and social environment of the animal to confirm the appropriateness and suitability of those conditions for the overall wellbeing of the animal. This combination of interventions is especially important for managing stress-associated conditions in cats, because any feeling of dis-ease, discomfort, danger, or perceived threat is likely to have a negative impact on the emotional state of the animal until those factors have been identified, address, and hopefully resolved.

Enrichment

Auditioning and maximizing enrichment opportunities is an indirect but highly impactful way to address feline stress, while keeping in mind that the preferences of one cat may be dramatically different from the next. Considerations may include ensuring the cat has appropriate outlets for energy and arousal, confirming the cat's ability to engage in species-typical behaviors, and providing adequate mental as well as physical stimulation to meet the specific animal's needs. It may be helpful to consider feeding routines, training opportunities, and even husbandry tasks such as brushing or grooming as enrichment opportunities.

Perceived Availability of Resources

Particular attention should also be made to the perceived availability of resources such as food and water stations, toileting locations, and safe resting places that allow the cat to retreat from social interaction if and when needed. It may be helpful to do a walkthrough (in-person or virtually) of the animal's living quarters to address any spatial “bottlenecks”, provide specific recommendations for maximizing three-dimensional space access, identifying and eliminating spatial “traps”, and customizing alternate access and egress paths throughout the environment. Much of this can be done via telemedicine platforms or through video capture by the client when in-person assessment of the environment is not practical for any reason.

Feline Training

Behavior modification strategies are absolutely available for cats, despite common pet owner perception to the contrary, and these can have a dramatic impact on stress-associated conditions. Cats follow all the same rules as other animals with regard to how they learn, which means that caregivers have the option of choosing approaches based on principles of habituation, classical conditioning, or the teaching of operant skills as they get started with active training. Specific skills such as targeting, stationing, relaxation/matwork, or trick training can all be leveraged depending on the goals and desired outcomes of training. Positive reinforcement-based training can have a meaningful impact on the cat's relationship with family members as well as their conditioned emotional response to the training environment, which may reduce stress both directly and indirectly. When making the transition to feline training from other species, there are several important considerations including the speed of food consumption and how that impacts the number of repetitions likely to be achieved within a given training session, opportunities for leveraging nonfood reinforcers such as various types of play, and ensuring that individuals are familiar with how to read body language to know when and if to progress training exercises to their next level of difficulty.

Nutritional Approaches to Stress

In addition to making sure that a cat's fundamental nutrient needs are being met, caregivers can choose food options that also include ingredients intended to reduce the overall stress level of the animal in a palatable, easily digestible way. Royal Canin Calm® is one such diet that is available in several varieties, including several "multifunction" dry/canned/wet formulations that are combined with ingredients that specifically support urinary, gastrointestinal, or mature cat health. If the magnitude of impact of this nutritional support is sufficient for an individual cat to recommend ongoing use, the ease of administration may dramatically improve long-term compliance of pet owners and without the added stress of additional pill, supplement, or medication related complications.

Supplement and Pheromone Interventions

There are many available supplement-based options on the market that are specifically tailored for cats, including Zylkene®, Solliquin®, Anxitane®, and Composure™/ComposurePRO™. Reasons for choosing one product rather than another may include flavor preferences of the individual cat, frequency of administration, availability of individual products in given consumer markets, and the overall response of the cat after trialing one or more products. While it is certainly recommended that practitioners familiarize themselves with the brands and products available to them in their market, and engage their product representatives with questions about usage of those individual products, it is also recommended that practitioners familiarize themselves with the active ingredients within each product, both for purposes of identifying replacement products if availability of one or more products is in question, as well as specifically targeting novel approaches when trialing a variety of product options (i.e. choosing one product for tryptophan supplementation, another for alpha-casozepine, and another for L-theanine content).

Several pheromone options are available as well, including products that mimic interdigital semiochemicals, facial compounds, and pheromones from the intermammary area (FeliScratch®, Feliway Classic® and Feliway MultiCat®, respectively). The delivery method for these treatments varies based on the individual product and may be valuable to consider given the "hands-off" nature of how these products are delivered to the environment rather than to the animal itself.

Pharmacological Interventions

The process of choosing whether or not to use medication and choosing which one to prescribe may vary from one patient to the next. However, using a systematic approach to medication selection may improve a practitioner's ability to achieve significant and repeatable results. It is important to first acknowledge the diagnosis or behavior pattern that is the target of intervention, with consideration for whether the behavior is likely to be motivated by fear, anxiety, stress, or arousal, and therefore more likely to be influenced by psychopharmacology. If the underlying motivation is something different than the ones listed here, such as insufficient exercise or an age-appropriate normal behavior pattern, medication support is not likely to be indicated and could in fact be contraindicated in some cases.

Assuming that medication therapy is appropriate for an individual patient, the next question is to consider whether situational/event medication use is more appropriate, or whether maintenance/daily medication options are a better fit. Situational medications may be appropriate when triggers are predictable, relatively infrequent, and the caregiver is able to reliably administer medication in advance of stimulus exposures. Maintenance medication options are more likely to be appropriate when the trigger exposure is frequent, unavoidable, or when adequate opportunity to provide medication support in advance of exposure is not routinely available.

The third question is to consider specific neurotransmitters such as serotonin, norepinephrine, or GABA, and their likely influence on the behavior pattern in question as a way of guiding therapeutic choices. Choosing one medication over another may also factor into account the type and likelihood of side effects, with awareness that in some cases side effects such as urinary retention (which can occur in response to SSRI therapies) could be problematic for an individual patient, or whether other side effects such as mild sedation could be advantageous in the early phase of treatment of other patients.

Stress Associated with Medication Administration

When considering medication or supplement use, pet owners should be questioned as to their ability to routinely administer the medication with ease and without significant stress or anxiety for the feline patient. In response to this question, if a client answers something along the lines of, "we'll get it in one way or the other...", their response should function as a red flag to the prescriber and a stopping point in the conversation to address other strategies that are likely to be more feline friendly. Even if client is able to administer the medication in the short-term, if the process is stressful for either the client or the animal, the likelihood of long-term success is reduced and the distress created by the medication administration routine may actually negatively impact the medication's therapeutic effect overall.

Strategies for reducing stress and improving reliability of medication administration include proactively teaching the cat to accept the medication and/or associating the medication routine with a high-value reinforcer, coaching owners on the physical mechanics of delivering medications in the most feline friendly way possible, and trialing various options for compounding. It may be necessary to try several different options before identifying the routine that works best for a given client and patient. It should also be noted that while many medications can be compounded into a transdermal preparation, this may not provide reliable absorption or therapeutic concentrations of the medication for every patient when used for behavioral medications such as SSRIs or other antidepressants. Clients should be made aware of options such as proactively creating a "snack time routine" that includes progressively larger doses of a therapeutic medication introduced into canned or other tasty food.

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Feline Behavior: More Than Just a Naughty Cat

Christopher Pachel, DVM, DACVB, CABC

Nuisance behaviors are generally considered to be normal behaviors that occur in problematic ways. They have the potential for creating an annoyance for pet owners and may sometimes pose danger to the animal themselves or to other individuals in the household. Although they certainly can create frustration and difficulties within the household, they are not generally “expressions of dominance”, or occurring due to vengeance or spite, as they sometimes are attributed to by owners or perhaps even individuals within veterinary or training communities.

It can be helpful to start with a few questions before providing recommendations for how to address these issues and patterns.

- Is the behavior normal for the animal or species?
- What interventions have been attempted to address the problem so far?
- What is reinforcing the behavior such that it continues or gets stronger?
- Does the owner have realistic expectations for improvement?
- Does the owner understand normal feline behavior?
- Does the owner have a basic understanding of learning theory and how to appropriately guide the process of behavior change?
- Does the household have the ability to implement the necessary management and training plan?

The answers to these and other questions may directly affect your assessment as well as the recommendations that you provide.

Fantastic resources exist to help owners determine whether they are providing an appropriate level of enrichment as well as a physical/social environment that meets the needs of their animal.

<https://www.catvets.com/public/PDFs/PracticeGuidelines/EnvironmentalNeedsGLS.pdf> - This document outlines the five pillars of a healthy feline environment, including:

- Provide your cat with a safe place
- Provide your cat with multiple and separated key resources
- Provide your cat with the opportunity for play and predatory behavior
- Provide your cat with positive, consistent, and protectable social interactions
- Provide your cat with an environment that respects the importance of his sense of smell

Translating these and other guidelines into practical recommendations generally involves first ensuring that the animal's biological and behavioral needs have been met. From there, the next step focuses on implanting management strategies and arranging the daily living environment in such a way that reduces or eliminates the animal's ability to rehearse the unwanted behavior. That is followed by implementation of treatment strategies such as teaching incompatible behaviors or providing feedback that renders the undesired behavior irrelevant or unproductive.

When choosing intervention options, practitioners should make a point of referring to the humane hierarchy of behavior change procedures (image provided within presentation). This hierarchy first emphasizes health, nutrition, and the physical setting, followed by antecedent arrangements and positive reinforcement, all of which should be considered and implemented prior to differential reinforcement of alternate behaviors or the use of potentially aversive strategies such as extinction, negative reinforcement, negative punishment, and certainly prior to the use of positive punishment.

Several of the more common “nuisance behaviors” for cats are scratching of furniture, climbing on counters, pouncing upon owners or family members, perceived hyperactivity, chewing and other destructive behaviors, excessive nocturnal activity, and vocalization or other attention seeking behaviors. Each of these patterns will be discussed in detail throughout the presentation, with an emphasis on understanding how to determine whether the behaviors are normal and appropriate for the animal, as well as discussion of appropriate and inappropriate intervention options.

Scratching of Furniture

This is considered a normal behavior that is observed in both clawed and declawed cats, which provides insight into the multiple functions of this behavior that include deposition of interdigital semiochemicals as well as enhancing the physical health of the animal. Care should be given to providing appropriately sized and positioned scratching posts,

with consideration for what most cats generally prefer as well as the preferences of the individual cat in question. Options for encouraging the ongoing use of suitable scratching substrates may include application of a pheromone-based product such as FeliScratch®. Other resources and educational tools can be found through sites such as <https://catvets.com/claw-friendly-toolkit/>. While deterrent options may appeal to the pet owner as a way of stopping or suppressing the unwanted behavior of scratching of furniture or other household items, these aversive interventions can have unintended consequences and are generally not indicated when other “cat friendly” methods have been proactively implemented.

Climbing on Counters

This is also a normal pattern and can occur for reasons such as height-seeking behavior or unintentional reinforcement, or may occur secondary to social tensions in the household and the cat finding comfort in avoiding close physical proximity to other household members. Strategies may include proactive training to shape the behavior into more acceptable alternatives, addressing underlying social tensions, or providing more desirable locations for the cat to climb and perch in the same general area as the counter on which the cat is climbing. As with other nuisance behaviors, the use of deterrents or punishment to suppress the unwanted behavior is generally not indicated or necessary and should be avoided.

Owner Directed Behaviors Such as Pouncing

Care should be taken to ensure that the cat’s fundamental needs for exercise and mental stimulation have been met, and that the cat is receiving appropriate reinforcement for desired behaviors (consistent with the previously mentioned hierarchy of behavior change) as this typically resolves or greatly diminishes the motivation to engage in this behavior. It may be helpful to explore a variety of enrichment opportunities to determine which is best suited to the preferences of an individual cat.

Hyperactivity

This may be raised as an owner concern, and an appropriate history should be taken to ensure that the energy level of the cat is consistent with other cats of a similar age prior to consideration of other differential diagnoses. This label is commonly given to young, active cats with insufficient outlets for their energy and with inadequate opportunities to engage in species typical behavior patterns. It may also be helpful to review the history for examples of accidental reinforcement by way of owner-attention that is given in response to the unwanted behavior. Strategies for engaging clients in the discovery process and capturing their motivation for providing additional enrichment opportunities can be an incredibly helpful aspect in addressing this concern!

Attention Seeking Behaviors

This term is used in situations in which the cat appears to be engaging in specific patterns due to historical reinforcement for the behavior, which may occur even when the owner’s intention may have been completely the opposite! For example, a cat that is relatively deficient in social contact from their caregiver may be accidentally reinforced by any attention or interaction that is given in a way that is contingent on the behavior the cat displays. In this way, even something that the owner intends to be punishing or aversive such as a verbal reprimand could functionally serve to strengthen the behavior. It may be helpful to observe multiple sequences of interaction between the cat and the owner to reliably determine whether this influence is at play within a particular household. It may also be helpful to evaluate the antecedent conditions under which the unwanted behavior is likely *and unlikely* to occur to establish the antecedent – behavior relationship that is relevant in that particular situation or household prior to making specific recommendations.

It is extremely common for pet owners to be given the recommendation to “just ignore” behavior they wish to see less of. While that is fundamentally correct that receiving less reinforcement for a specific behavior should have the influence of decreasing the frequency or intensity of the pattern, it is also likely that the animal with a learning history of being rewarded for a specific behavior will display an “extinction burst” (display the unwanted behavior with *greater* frequency or intensity prior to trialing other response options) if the behavior is subsequently ignored. And, if an owner is not counseled appropriately about this possibility, it’s possible that attempting to ignore the behavior could actually *worsen* the problem over time if a response or reinforcement is given for the new and more intense version of the behavior. The likelihood of this outcome is significantly reduced if the animal is first reinforced for an alternate behavior prior to the ignoring strategy being implemented. This approach greatly reduces frustration on the part of the learner and is in greater accordance with the hierarchy of behavior change principles.

Additional questions such as whether the behavior occurs in the absence of the owner, whether the behavior is more likely to occur in close proximity to a particular family member, or whether the behavior appears to be increasing subsequent to attempted interventions should all be considered while evaluating for an attention-seeking motivation.

It should be noted that understanding the guiding principles of behavior change is a significant part of any intervention plan for feline nuisance behaviors. And, as much or more attention should be paid to interview and communication strategies that increase the likelihood of an owner first understanding and then being willing to implement recommendations as they are given. Examples will be provided and discussed throughout this presentation to guide the practitioner in sharing these recommendations with clients and pet owners.

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Feline Hypersensitivity Dermatitis: Understanding Cause & Therapy

Michael A. Rossi, DVM, MNS, DACVD

Introduction

Feline hypersensitivity dermatitis (FHD) is a relatively common presentation in the veterinary clinic. The feline patient often presents as a very challenging and frustrating case to the veterinary clinician. The clinical signs of the disease are often confusing and are not pathognomonic for any single underlying etiology. It is for these reasons that an accurate, timely diagnosis and a successful, comprehensive treatment plan are essential, but can be difficult to manifest. Many pet owners seek out immediate relief, but fail to understand that this condition is a life-long struggle for their pet. It should be paramount that the veterinary clinician be able to identify clinical signs consistent with FHD and then determine which treatment plan is best for the individual case.

Cutaneous Reaction Patterns in Felids

The veterinary clinician should be able to distinguish between the more common reaction patterns seen in cats with FHD. While none of these patterns are indicative of one specific underlying etiology, they should suggest that the individual patient has a hypersensitivity disorder and that further investigation into this is warranted. What all four common reaction patterns have in common is that the patient is experiencing some degree of inflammation and pruritus. The four cutaneous reaction patterns in cats are: i) self-induced alopecia, ii) head/neck/pinnal pruritus, iii) eosinophilic granuloma complex (indolent ulcers, eosinophilic plaques), and iv) miliary dermatitis.

Underlying Etiologies in FHD

There are three main allergic dermatoses found in the feline species: flea bite hypersensitivity, cutaneous adverse food reactions, and environmental allergies. Clinically, these three conditions can present with identical signs. It is for this reason that a good history and a thorough clinical examination are imperative. The data collected with these two activities will help to lay the foundation of the treatment plan for the patient. Feline patients differ from their canine counterparts in that there is substantially more information documented in dogs regarding hypersensitivity disorders. The following information is broken down into the individual etiologies:

I. Flea Bite Hypersensitivity:

Flea bite hypersensitivity (FBH) has been implicated as the trigger factor in the vast majority of cases of FHD. The incidence of FBH in patients exhibiting at least one of the cutaneous reaction patterns described above has been reported to be as high as 70% in one study. This is often dependent on the area of the country where the patient resides, as FBH is more common in flea endemic regions. It is often difficult to find evidence of fleas on the feline patient as they are meticulous groomers. The production of pro-inflammatory cytokines seen with FBH in cats is due to a salivary protein termed flea salivary antigen 1. The introduction of this protein into a sensitized individual will lead to a type I (immediate-type) and/or type IV (delayed-type) hypersensitivity reaction. Treatment should be focused around preventing exposure to the antigen and reduction of inflammation. The isoxazoline class of drugs work by antagonizing ligand-gated chloride channels and is the author's prevention of choice. These products are often applied topically and on a monthly basis to provide sustained protection against the reintroduction of antigens. It is important to treat all animals in contact with the patient as they could be asymptomatic carriers of fleas. Environmental decontamination could also be considered. Glucocorticoids, such as prednisolone administered at 1 mg/kg once daily or a methylprednisolone injection administered as 20-40 mg/cat, or oclacitinib 0.7-1.2 mg/kg every 12 hours (extra-label use) are effective at reducing pruritus and providing comfort in these patients and should be used short-term.

II. Cutaneous Adverse Food Reactions:

The incidence of cutaneous adverse food reactions (AFR) in cats varies greatly in the reported literature. In general, the reported incidence is between 1-6% of feline patients. It is the author's opinion that this condition is likely underreported and/or underdiagnosed. As with canine patients, the pathogenesis of AFR in cats is not completely understood. There are varying reports pertaining to what extent there is allergen-specific IgE involvement, as well as the exact type of hypersensitivity reaction identified in cases. The patient will typically present with a non-seasonal pruritus in the case of strict AFR. Again, there may be the presence of one or more of the previously noted cutaneous reaction patterns. Clinical signs may include gastrointestinal disturbances in up to 33% of feline patients presenting for AFR. Unusual clinical signs have been noted in some patients, including plasma cell pododermatitis, conjunctivitis, and respiratory abnormalities. The diagnostic of choice for this condition is a strict elimination diet trial. The most commonly reported food allergens in cats with AFR are beef, dairy products, chicken, and fish. Together, these groups account for roughly 90% of documented cases of AFR in cats from various reports. Once the patient has been fed the strict elimination diet trial and clinical resolution of lesions has been obtained, the patient is then fed a provocation diet to confirm suspicion of the underlying cause. Serum allergy testing, intradermal allergy testing, and gastroscopic testing

have all been shown to be inaccurate in the cat. The elimination diet trial should be kept strict throughout the duration. It is cited in the literature that more than 80% of cats with known AFR showed resolution within 6 weeks of beginning a strict elimination diet. That percentage increased to almost 90% by the 8 week time point. It is generally recommended that an elimination diet last between 8-12 weeks. There are many commercially available diets containing limited ingredients and novel proteins that can be utilized. A home-cooked diet may also be used provided that the owner works with a veterinary nutrition expert to ensure that the diet is balanced. As the diet trial may last several weeks, control of pruritus is paramount and consideration should be given to treatment options that are safe for that time period. Glucocorticoids and/or modified cyclosporine at 7 mg/kg once daily are effective at controlling the pruritus during the diet trial. Oclacitinib may also be attempted, but is not very effective for this condition in the author's experience.

III. Environmental Allergies:

Environmental allergies in the feline patient can present with either a seasonal or non-seasonal course. The terms "feline atopy" and "feline atopic dermatitis" are now defunct and have been replaced with the term non-flea, non-food induced hypersensitivity dermatitis. This is due to the fact that there is a lack of conclusive allergen-specific IgE involvement, which is the hallmark of true atopic dermatitis as seen in both the dog and man. While it has been noted that there is an increase in CD4+ T cells in the skin of allergic cats, the cytokine profile that accompanies this condition is still under investigation. The vast majority of these patients present with varying degrees of pruritus surrounding the times of allergen exposure. As previously discussed, the feline patient may present with at least one of the cutaneous reaction patterns. Environmental allergies are typically a diagnosis of exclusion, so it is often arrived at once flea bite hypersensitivity and adverse food reactions are ruled out. Along with the cutaneous manifestations of the disease, the patient may also present with signs of feline small airway disease, such as allergic rhinitis or sinusitis. Sneezing may be a prominent finding in cases of environmental allergies in cats with some reports approaching nearly 50% of patients with the condition. Unlike the canine patient, bacterial and/or fungal infections of the ears and skin are uncommon to rare in the feline patient with environmental allergies. This may be related to the reduction in adhesion of the microbes to the feline corneocytes.

The goal with therapy for feline patients with environmental allergies is to decrease the frequency and severity of the allergic flares as safely as possible. A cure should not be expected and this should be relayed to the owner early in the treatment plan. Treatment should be evaluated on a case-by-case basis to determine which modality is best for that individual. Conservative treatment plans should revolve around antihistamines, although success rates remain relatively low with this modality. Medications, such as cetirizine 5 mg per cat given once every 24 hours, should be tried for a minimum of two weeks to determine efficacy. More aggressive systemic therapy may consist of glucocorticoids (prednisolone 1-2 mg/kg every 24 hours and then tapered) and/or modified cyclosporine (Atopica 7 mg/kg every 24 hours). These therapies should be used at as low of a dose and for as briefly as possible to provide comfort. Allergen-specific immunotherapy (ASIT) remains the treatment of choice for feline patients with environmental allergies. Allergens are identified using intradermal allergy testing and/or serum allergy testing and then formulated into either a subcutaneous injection or a sublingual drop. Response rates vary, but most of the literature places them between 70-80%. ASIT should be given for at least 12 months to determine if this form of therapy will be effective and administration may be tapered at that point.

Conclusion

There is still much that remains unknown when evaluating the pathogenesis of FHD. There also appears to be considerable overlap of clinical signs amongst the known etiologies, making the determination of the underlying cause difficult and frustrating for the veterinary clinician. The cause of the cutaneous manifestations of the condition should be ruled out in a consistent, methodical manner until the correct diagnosis is discovered. Treatment should focus on the underlying issue(s) while providing relief through systemic and/or topical medications. It is important that the treatment not be made worse than the disease itself. The goal of the comprehensive treatment plan is to improve the quality of life for the feline patient and the pet owner.

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Role of Probiotics in the Management of Diarrhea in Cats

Michael Lappin, DVM, PhD, DACVIM

Introduction

Probiotics are live microorganisms that when administered in adequate amounts confer a beneficial health effect on the host.¹ Prebiotics are supplements or foods that stimulate the growth or activity of endogenous intestinal microorganisms. Products that contain both prebiotics and probiotics are called synbiotics.

There have been many studies and reviews of the effects of probiotics or synbiotics on the health of humans, but fewer in small animals, particularly cats.^{1,2} Overall, the amount of evidence supporting the use of probiotics or synbiotics for the treatment of any feline clinical problem, including diarrhea, is small. However, the information supporting the use of probiotics in cats is generally strongest for managing gastrointestinal syndromes such as acute or chronic diarrhea. There is also some evidence that probiotics might be beneficial for mitigating antibiotic-associated vomiting or diarrhea or constipation. It is known that some probiotics help balance the endogenous microbiota and that some can inhibit replication of pathogenic bacteria. Some of the proposed mechanisms of action include competition for essential nutrients or receptor sites, binding of pathogenic bacteria, and production of inhibitory substances. There is also evidence that some probiotics induce immune modulating effects with potential benefits for the management of inflammatory bowel disease, atopy, or infectious diseases with systemic involvement (e.g., feline herpesvirus-1).³

It is also now known that some probiotics can beneficially influence innate and acquired immunity systemically. Not all of the methods by which probiotics modulate the immune system have been characterized, and it is likely that these effects vary by probiotic. Thus, a clinical effect that is shown to be induced by one probiotic may not be induced by others, even in the same genus and species of bacteria. For example, there are many strains of *Enterococcus faecium*, but positive clinical effects in cats have only been shown with the *E. faecium* strain SF68.³

While probiotic use is generally considered safe, consumers should ask companies marketing probiotics for the product's safety information. One of the other major issues concerning probiotic use in small animal practice is quality control. In two veterinary studies, the majority of products claiming to contain probiotics generally did not meet the label claim when evaluated.^{4,5} Other unresolved issues for probiotic use in small animals is the optimal number of bacteria to be used and whether there are clinical benefits to having multiple strains of bacteria in a product. Since each bacterium in a probiotic can have unique effects, products containing multiple bacteria may actually have competing mechanisms of action lessening potential beneficial effects.

There are several veterinary probiotic products marketed in the United States that have been shown to be safe, meet label claims, and have clinical studies supporting potential beneficial effects, including *E. faecium* strain SF68 (FortiFlora®, Nestlé Purina PetCare). Recently, studies evaluating gastrointestinal effects of other commercially available probiotics or synbiotics have been published and can be used to help veterinarians choose which products to make available to their clients. Of course, there are other probiotics specific to different countries. If you are planning to buy a new probiotic for your clinic, ask the manufacturer to see their stability data and any efficacy data they may have.

Feline studies using commercially available probiotics or synbiotics in the United States

In one of the first studies of a probiotic in cats, *E. faecium* strain SF68 was shown to be safe in healthy kittens and induced evidence of immune modulation.⁶ To determine whether the immune modulating effects of noted in the healthy kitten trial could be of clinical benefit, we chose to study FHV-1.³ In this pilot study, it was hypothesized that supplementing *E. faecium* strain SF68 would stabilize the fecal microbiome as well as decrease the incidence and severity of clinical disease, the frequency of episodes of FHV-1 shedding, and the total number of FHV-1 DNA copies shed over time in cats with chronic FHV-1 infection.

Twelve cats with chronic FHV-1 infection were supplemented with either *E. faecium* strain SF68 or a palatability enhancer as a placebo. Clinical signs of disease, FHV-1 shedding, FHV-1-specific humoral and cell-mediated immune responses, and changes in the fecal microbiome were monitored and evaluated. After an equilibration period, mild stress was induced over time by changing the cats' housing from cages to group housing multiple times over a five-month period.

Fecal microbial diversity was maintained throughout the study in cats supplemented with *E. faecium* strain SF68, but diversity was decreased in cats supplemented with the placebo, indicating a more stable microbiome in the treated

cats. These results supported the hypothesis that this probiotic could have favorable effects on diarrhea in cats. While the cats in the current study did not have diarrhea, the cats supplemented with *E. faecium* strain SF68 had significantly fewer episodes of conjunctivitis than the placebo group during the supplementation period, suggesting that probiotic administration lessened morbidity associated with chronic FHV-1 infection exacerbated by stress.

In another study, it was hypothesized that cats housed in an animal shelter that were supplemented with *E. faecium* strain SF68 would have decreased episodes of diarrhea and improved fecal scores compared with untreated cats in the same environment but housed in two different rooms.⁷ The cats were all fed a standardized diet and animals in one room were supplemented daily with *E. faecium* strain SF68 and animals in the alternate room were supplemented daily with a placebo. Prior to cleaning the room each morning, feces in the cage of each cat was scored by a masked investigator using a standardized scoring system.

The percentage of cats with diarrhea for two days or longer was 7.7% for the probiotic group and 20.7% for the placebo group.⁷ This result was significantly different ($p = 0.0297$) and suggests that administration of *E. faecium* strain SF68 to cats housed in shelters may lessen the numbers of days with diarrhea.

Amoxicillin-clavulanate is frequently prescribed by veterinarians for a wide variety of feline conditions, including bite wound abscesses and upper respiratory infections. As the drug has a broad spectrum against many bacteria (including anaerobes), diarrhea, vomiting, and loss of appetite can occur when administered to cats. One objective of a recently published study was to quantify the frequency of gastrointestinal signs induced by amoxicillin-clavulanate.⁸ The second objective was to determine if supplementation of *E. faecium* strain SF68 could ameliorate these side effects as this probiotic has been shown to be effective in the management of diarrhea in cats. All cats were administered amoxicillin-clavulanate (Clavamox®; Zoetis) at 62.5 mg/cat orally twice a day for seven days. Two hours prior to the antibiotic administration, cats were fed one-quarter can of canned food mixed with the dose of *E. faecium* strain SF68 that was equivalent to a commercial probiotic product (13 cats) or only the palatability enhancer used in the same commercial product (placebo; 14 cats). Supplementation of the placebo or *E. faecium* strain SF68 and clinical fecal scoring were continued for an additional five days after stopping the antibiotic.

Fecal scores > 5 on a seven-point scale were detected in nine of 13 cats (69.2%) in the treatment group compared with 12 of 14 cats in the placebo group (85.7%).⁸ Fecal scores of 7 were only detected in the placebo group. When compared, the cats in the treatment group had significantly lower total fecal scores than the cats in the placebo group for days one through 11 ($p = 0.0058$). The results show that administering amoxicillin-clavulanate orally to cats can induce vomiting or diarrhea and can alter the gastrointestinal microbiome. In addition, supplementing the probiotic *E. faecium* strain SF68 can lessen some associated clinical abnormalities.

After the previously described study was completed, *Enterococcus faecium* SF68 was combined with psyllium as a prebiotic and marked as a synbiotic (FortiFlora® SA Nestlé Purina PetCare). The following is an abstract presented at the American College of Veterinary Internal Medicine Annual Forum in 2020.

Diarrhea is a common and potentially significant complication in cats undergoing antibiotic therapy. Data supporting the benefit of supplementing probiotics or synbiotics to cats with antibiotic-induced diarrhea has started is lacking. This study examines effects of supplementing a synbiotic (*Enterococcus faecium* SF68 and psyllium) to cats with pre-existing antibiotic associated diarrhea.

Sixteen healthy, young-adult research colony cats fed a commercial dry food were administered amoxicillin-clavulanate (Clavamox) at 62.5 mg/cat twice daily. Using a standardized fecal scoring system, trained, masked personnel scored feces every twelve hours, with scores >4 considered diarrhea. Clavamox was discontinued if fecal scores were >4 for 2 days. Cats were then randomized into 2 treatment groups, one supplemented with the synbiotic in 15g of canned food once daily, the other supplemented with the palatability enhancer from the synbiotic in 15g of canned food once daily.

Diarrhea was less severe overall in the probiotic group, with 24.5% of fecal samples scored >5, compared with 48.9% in the control group ($p = 0.0132$). Time to diarrhea resolution was 4.5 periods from initiation of treatment in the probiotic group, compared with 6.5 periods in the control group ($p = 0.472$). Clinical resolution of diarrhea was achieved in all cats in the synbiotic group. Two cats in the control group had a rescue protocol instituted for diarrhea that failed to resolve during the study period.

These results indicate that supplementing this synbiotic to cats with diarrhea provoked by administration of Clavamox reduces severity of diarrhea and may decrease time to resolution.

Other notable studies with probiotics or synbiotics marketed in the United States include an open trial showing potential clinical benefits of including a synbiotic for management of chronic diarrhea in cats¹⁰ and use of a synbiotic to lessen vomiting in cats administered clindamycin.^{11,12} In addition, data from an *in vitro* study suggested that 2 different enterococci-containing probiotics might be of benefit in the management of *Tritrichomonas foetus* diarrhea in cats.¹³

Overall, the evidence gathered to date suggests that various probiotics or synbiotics may be of benefit in the management of certain clinical abnormalities in cats, including diarrhea. However, additional data is needed to help prove mechanisms of action of the various products. As more information concerning use of probiotics and synbiotics for the management of feline diarrhea and other diseases is gathered, veterinarians should seek out products that have been proven to be safe, to meet the label claims, and to have a high level of evidence of clinical efficacy.

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Spring into Feline Medicine



THREE-DAY **VIRTUAL LIVE CE EVENT**

Sunday, April 18th | Wednesday, April 28th | Saturday, May 8th

ALL TIMES ARE EASTERN TIME ZONE

Sunday, April 18, 2021

TIME	SESSION TITLE	SPEAKER	SPONSOR
12:00 - 1:20 pm	Top Tips for Management of Stress-associated Conditions in Cats	Dr. Christopher Pachel	 ROYAL CANIN
1:40 - 2:40 pm	Feline Behavior: More Than Just a Naughty Cat	Dr. Christopher Pachel	 ROYAL CANIN
2:50 - 3:50 pm	Feline Hypersensitivity Dermatitis: Understanding Cause & Therapy	Dr. Michael A. Rossi	 CEVA
4:00 - 5:00 pm	Role of Probiotics in the Management of Diarrhea in Cats	Dr. Michael Lappin	 MERIAL PRO PLAN VETERINARY DIETS

Wednesday, April 28, 2021

TIME	SESSION TITLE	SPEAKER	SPONSOR
12:00 - 1:20 pm	Peak Cat Care: Getting the Most from your Feline Exam	Dr. Elizabeth Colleran & Dr. Margaret Gruen	 ZOETIS PETCARE
1:40 - 2:40 pm	Cutting Edge Updates on Chronic Kidney Disease: Understanding Dietary Phosphorus & Renal Health	Dr. Jonathan Elliott	 ROYAL CANIN
2:50 - 3:50 pm	Cutting Edge Updates on Chronic Kidney Disease: Bone Mineral Disturbances – What Do We Know & Why Does it Matter?	Dr. Jonathan Elliott	 ROYAL CANIN
4:00 - 5:00 pm	Learning the Ins & Outs of Taking Feline Blood Pressure Without Elevating Yours	Ms. Ellen Carozza & Dr. Kelly St. Denis	 Boehringer Ingelheim

Saturday, May 8, 2021

TIME	SESSION TITLE	SPEAKER	SPONSOR
12:00 - 1:20 pm	Keeping Felines Feisty Despite Frailty	Dr. Sheliah Robertson & Dr. Bonnie Wright	
1:40 - 2:40 pm	Nutritional Myths: Cat Owner Questions & Concerns	Dr. Julie Churchill	 Hills Transforming Lives
2:50 - 3:50 pm	Complicated Endocrine Cases	Dr. Cynthia Ward	 Dechra Veterinary Products
4:00 - 5:00 pm	Secrets to Managing Today's Diabetic	Dr. Cynthia Ward	 Boehringer Ingelheim

Peak Cat Care: Getting the Most from your Feline Exam

Elizabeth Colleran, DVM, MS, DABVP (Feline) & Margaret Gruen, DVM, MVPH, PhD, DACVB

Video as an Extension of the Physical Exam

Detection of orthopedic pain in cats is difficult, to say the least. This is, in part, due to cats' behavior in the clinic, and our inability to observe cats as they move through their environment. Anxious and fearful cats often hold their body close to the ground with all four feet planted firmly on the floor in a ventral flat posture. The feet are often under the body and therefore not visible and the pads are usually in contact with the surface they are on. Such a posture protects vulnerable areas such as the belly as well as ensuring the cat is in a position for quick retreat if needed. They may also have their tail clamped tightly, wrapping closely around the body; in some instances, it is tucked under the body so is not visible – most likely, to protect it from any potential harm. They are also hesitant to move, and if they do move, they may keep their bodies low to the ground, making assessment of gait nearly impossible.

Research has also highlighted the behaviors that are most likely to be affected by chronic arthritic pain; along with changes in mood and affect, these include: jumping up, jumping down, climbing stairs, going down stairs, running, and playing with toys. It's obvious right away that these behaviors are difficult to observe in most cats during a visit to the clinic. Even with our most feline friendly techniques, many cats will simply not perform these activities in the clinic, or will do so with postural changes that are difficult to interpret.

This makes home-video an essential tool in observing cat behavior and mobility. What was once a chore filled with tiny discs or cartridges and hours of film is now as easy as a button on most phones. Owners can be instructed to film these behaviors (jumping up/down, going up/down stairs, etc.) in the home for us to observe in the clinic. While these can be incredibly helpful as part of our exam, their utility is limited by the quality of the video and the length of the clip. Owners tasked with getting video without further instruction may, despite best intentions, produce videos that are not useful.

To obtain the best (i.e., most useful) videos, there are a few instructions for owners that we have found produce the best results:

1. **Choose an open, well-lit area.** Make sure your cat does not blend into the background as he/she moves around.
 - o Do not video a black or brown cat against a dark wall or a shadowy area, for example
 - o Natural light is preferred, or a room or area with good overhead lighting
2. **Camera angles.** If possible, take a video to show a **full side view** of your cat's body. Try to keep your cat's legs and body in the frame. You may have to take the video standing back slightly to frame your cat with enough room to move.
 - o Show your cat in motion, from the side, on screen.
 - o Avoid frontal/head-on angles (you will only see your cat's face or rear; walking directly toward or away from the camera).

Your cat is a character with an expressive face, **but we need to see the body** to find out if he/she is having difficulty doing certain movements.

Tip: If taking the video on your phone, turning the phone sideways (landscape) can help show off the full body.

3. **Actions/behavior to capture:**

It's important to clearly capture one or more of these movements in your video to find out whether your cat may be in pain:

- o ***Climbing up stairs***
- o ***Going down stairs***
- o ***Jumping up to a chair or table***
- o ***Jumping down from a chair or table***

Optional activities

- o Running
- o Chasing objects, preferably on a flat surface

If you can capture your cat performing the same behavior at least 3 times, that would be very helpful. It could be in separate videos or in the same continuous video.

Tip: You might want to have a favorite toy or treat ready to encourage your cat to do the action.

4. **Cut to fit:**

Each of these behaviors may take only a few seconds, but may be captured in the middle of additional footage. If possible, edit your clips to show only the behavior of interest as this will maximize our ability to assess your cat's movements.

Using In-Home Video as Part of Your Cat Friendly Comprehensive Physical Examination

Good observational skills are very important in facilitating the identification of behaviors, body language and posture associated with an emotional response. There are many elements to assess: what behavior the cat is seen performing, what vocalizations it is making (eg, meowing, hissing, growling, purring), what posture the cat is in (eg, crouched, standing tall, tensely rolled on side exposing belly), and what different parts of its body are doing (eg, the position of the ears; how the tail is being held in relation to the body, whether it is moving and, if so, at what speed). There is a lot of information to process all at once and this takes a great deal of practice as well as close attention to detail.

Acute stress progressing to acute DIStress is commonly seen in feline patients during veterinary visits. Differentiating between stress and disease is critical to prevent erroneous diagnoses and unnecessary treatments. The differential diagnosis must consider both emotional and physical health. As many physical and diagnostic findings can occur with both physical and emotional conditions, client history, patient body postures and facial expressions must also be considered to differentiate between physical and emotional health.

Specific techniques that can change the lifelong response of a cat and caregiver to regular feline health care will be demonstrated, including:

- COVID-related changes to daily operations that can be modified to improve the experience
- Distraction and acupressure rather than restraint
- Sedation rather than forceful restraint for radiographs
- Blood collection, cystocentesis, nail trimming, and blood pressure measurement towel techniques that reduce stress

These techniques will assist in assessment of chronic pain in cats, and facilitate observation of behaviors in the clinic. The review of in-home video can also help identify cats with mobility impairment, observe the particular behaviors that are impaired, and target the orthopedic examination. The orthopedic examination then encompasses not just our flexion and extension of joints, but extends the exam from the home to the clinic. Cats whose videos show signs of mobility impairment can be further examined through observation, performance tests, and hand-on orthopedic examination. Performance tests take advantage of cats' behavior in the clinic; easiest is to observe them jumping down and walking (often toward their carrier). More difficult is the observation of jumping up, but some cats can be enticed to jump onto chairs, benches, or ottomans in the clinic setting.

When reviewing video, a standardized scoring system can be used to allow comparison across clinicians and to monitor progression and response to treatment. While these are in development, even a "normal-mild-moderate-severe" impairment scale for each behavior is helpful. Using the standardized set of behaviors also allows clinicians to become comfortable with the range of impairment as the same behaviors are observed over time.

Create Compliance While Balancing a Multimodal Pain Management Plan and Protecting the Relationship of the Caregiver and Their Beloved Cat

As veterinarians and support staff, we are often dismayed and disappointed when a treatment plan that we have created for a patient meets resistance from a caregiver. Our view of their lack of compliance is that they must not understand the importance of our plan. The challenge is not a better explanation but a better understanding of the impact some interventions may have on the relationship between cat and caregiver, the emotional price of medical care to both parties.

When the balance between protecting the relationship and successfully treating a condition or illness is included in the planning process, better outcomes can be confidently anticipated.

The cat is far more difficult to evaluate for chronic pain because of their evolution as solitary hunters. They need a smaller repertoire of inter- and intra-species social communication compared with the dog. Cats are often described as "aloof" and "independent" which could stem from the lack of obvious facial expressions and visually expressive characteristics of the dog.

Their need to express themselves is diminished by their independence. Cat communication has been largely overlooked as it lacks the drama and intensity of dogs. Cats in the wild live alone and must compete with each other for food and other resources. Cats are deliberately inscrutable. Letting on that a good meal is nearby or that a safe resting place has been discovered will not result in a good outcome for that cat. Conversely, letting on that one is injured, sick or exhausted may lead to becoming another's prey. The subtlety of signaling has led to a misunderstanding of the signs that health interventions are required to preserve a great quality of life.

Quite often the subtlety of pain signaling in the cat stands in the way of a pain management plan. When caregivers don't believe it is present, they will not act. A "pain trial" is a powerful way to overcome this resistance. A 3-7 day course of meloxicam has become a standard for demonstrating behaviors cats still want to perform but are not comfortable enough to do so.

Cats given an NSAID may resume:

- Jumping on the bed to sleep with caregiver
- Sleeping through the night
- Engaging in play
- More engagement with caregivers – brushing, cuddling

Once these changes are appreciated by caregivers, they delight in the restoration of their beloved cat's companionship and readily welcome a pain management plan.

Once an understanding of the signs of pain in cats has been conveyed and the importance of its control understood by caregivers. A plan for treatment of OA pain that balances the goals of the caregiver can be created. These goals go beyond the successful management of pain and include the preservation of the loving relationship between cat and caregiver. The home range for the cat is a place of predictability and safety so that change is tolerable. When actions are taken by the caregiver that cause stress or fear in the cat, the relationship can be grievously harmed by the event. Many issues of compliance with medical recommendations come down to the erosion of relationship. When the cat who slept routinely with the owner, now hides under the bed when approached by the caregiver, the emotions for both parties are harmed. The caregiver feels sad or guilty and the cat feels fear or anxiety.

Thus, the plan must be one that considers the ability and commitment of the caregiver, cost of care, the availability of resources. The owner will be more likely to embrace the suggestions in a multimodal pain management plan if they feel really involved in its formulation, if the goals and objectives are important to them, and if they don't feel pressurized, tested or judged. How the owner approaches the task will differ from one individual to another. Nurturing the trusting relationship between caregiver and veterinarian will simplify planning.

Components of multimodal pain management that will be easily tolerated include:

- Small volume medications that are either palatable or can be made palatable,
- Supplements or medications that can be added to high value treats (Churro, babyfood) and delivered gently via syringe,
- Classical conditioning – tolerance/reward training,
- Adding warmth to the cat's resting places,
- Therapeutic technology that is not irritating – laser, Assisi (PEMF) loop, and
- Environmental modifications to improve access to high-value places in home.

Future forms of therapy for OA in cats will always need to balance efficacy with the beloved relationship people and their cats enjoy. Creating this awareness now will drive innovation in the future toward pain management interventions that are effective and tolerable to both cat and caregiver.

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Cutting Edge Updates on Chronic Kidney Disease: Understanding Dietary Phosphorus & Renal Health

Jonathan Elliott, MA, VetMB, PhD, DECVPT, MRCVS, FHEA

Introduction

The balance between phosphorus intake and its excretion on a daily basis in a skeletally mature mammal is achieved through a complex interplay between the gut, the bone and the kidney. Movement of both calcium and phosphorus into the system from the gut and between complexed stores and extracellular fluid and their excretion via the kidney are processes which are regulated via hormones. Our understanding of the major hormones and their interactions has increased significantly over the last 20 years. This understanding is beginning to impact on how we formulate diets and diagnose and manage diseases, including kidney disease.

Major Players in Phosphate Homeostasis

Until the year 2000, the major hormones thought to influence phosphate homeostasis were those primarily concerned with calcium balance, namely parathyroid hormone (PTH) and calcitriol. PTH increases phosphate excretion via the kidney but, at the same time, brings more phosphate into the system by increasing calcium and phosphate release from bone and increasing calcitriol formation. Calcitriol acts on the intestine to increase both calcium and phosphate absorption and is synergistic with PTH in its actions on the kidney and bone. It was postulated a hormone existed that increased renal excretion of phosphate without releasing phosphate from bone or increasing phosphate absorption from the gastrointestinal tract. That proved to be the case with the discovery of FGF23, a phosphatonin that inhibits (a) the expression of the proximal tubular phosphate transporters (thus increasing renal excretion of phosphate), (b) PTH secretion and (c) the conversion of calcidiol to calcitriol by the kidney^[1]. As with many hormones, its discovery came about because of diseases recognised where excess hormone occurred, such as X-linked hypophosphatemic rickets^[2].

FGF23 is produced by osteocytes and osteoblasts. The exact stimulus for its secretion remains to be determined. Acute ingestion of phosphate in cats does not lead to increased FGF23 secretion^[3] but chronic ingestion of increased amounts of phosphate does lead to elevated circulating levels of FGF23^[4,5]. There is still much to understand about phosphate homeostasis in the cat. The pathways for intestinal absorption and factors influencing these remain completely unknown for example. These vary between species and so characterisation of the feline phosphate transporter systems seems to be an important goal for future research.

Evidence That Feeding Too Much Inorganic Phosphate Can Harm the Kidney

The Evidence in Human Medicine

Nutritional recommendations tend to focus on the minimum recommended daily intake of nutrients. In human medicine, concern over the adverse health effects on the cardiovascular, skeletal and renal systems of intake of foods containing excess (added to preserved foods) phosphorus, particularly when added in highly available inorganic form in excess of calcium such that the ratio of calcium and phosphorus falls below 1:1 has been raised^[6]. Intake of phosphorus well above the adult recommended daily allowance of 700 mg/day is commonplace in the US particularly where processed foods make up a substantial proportion of the diet. The ability to assess accurately dietary intake of phosphorus is hampered by the lack of requirement for manufacturers to specify the amount of phosphorus added to processed foods and drinks.

The inability to assess accurately dietary phosphorus intake in people has meant much of the epidemiological data associating adverse health events at the population level with phosphorus is based on serum phosphorus concentration^[7]. Because much of the body's phosphorus is located intracellularly or bound in structural tissues of bone (albeit able to move between these locations and extracellular fluid, including blood), fasting serum phosphorus may be a relatively insensitive indicator whole body overload with phosphorus or excessive dietary intake. Thus, when using serum phosphorus to indicate excess dietary intake, large populations need to be studied and differences are demonstrated even though the vast majority of the population have serum phosphorus concentrations within laboratory reference intervals. This is further complicated by circadian variation in serum phosphorus concentrations regardless of dietary phosphate intake. Nevertheless, chronically elevated phosphorus intake is associated with increased circulating concentrations of PTH and FGF23. Elevation of these hormones is, in turn, associated with increased risk of cardiac muscle hypertrophy, vascular calcification, hypertension and therefore risk of adverse cardiovascular outcomes^[7]. Furthermore, elevated serum phosphorus concentrations in people with normal kidney function is associated with increased risk of adverse cardiovascular outcomes of stroke, coronary heart disease and death^[8].

The role of excess phosphorus intake in initiating kidney disease in people is difficult to disentangle from its association with progressive renal injury once kidney disease is established (see lecture 2). In the human literature, an epidemiological study involving 28,500 people undergoing health screening demonstrated that serum phosphorus above 3.5 mg/dl is associated with increased risk of developing end stage renal disease (per 1 mg/dL increase: aHR 1.40; 95% CI, 1.32–1.47; $P < 0.001$)^[9]. Similar results were obtained from a retrospective study of an ethnically diverse population of 94,989 people undergoing health screening in southern California with 11 years follow-up^[10]. However, prospective intervention studies have yet to be undertaken in human populations to demonstrate cause and effect of these observed associations. The most common underlying disease leading to chronic kidney disease in humans is diabetes and these studies adjusted for that risk factor although other published data has shown serum phosphorus was not linked to adverse renal outcomes when individuals with diabetes are excluded.

Acute feeding studies involving human subjects have demonstrated that ingestion of a meal containing excess highly available phosphorus is associated with cardiovascular effects. In a double blinded cross-over study involving 11 healthy male volunteers, intake of 1200 mg of phosphorus led to reduced flow mediated vasodilation, a non-invasive measure of endothelial cell function, an effect which was related to the increase in serum phosphorus 2 hours after the meal ingestion^[11]. This suggests reduced ability of the large arteries in the body to produce nitric oxide, an effect that can be mimicked in vitro by increasing phosphate concentrations in the medium bathing blood vessels.

The Evidence in Feline Medicine – Experimental Studies

The body of evidence suggesting that excess phosphorus intake damages the kidney is supported by experimental animal studies, including studies involving cats. In assessing dietary requirements of phosphorus in mature ovariectomised healthy cats, Pastoor et al., (1995)^[12] noted reduced glomerular filtration rate (GFR) measured by endogenous creatinine clearance following 4 weeks of intake of diets with a phosphorus content of 27.7 mmol/MJ. Dobenecker et al (2018)^[13] fed adult cats a maintenance diet supplemented with sodium and calcium monophosphates to deliver 3x maintenance amounts of phosphorus for 29 days. This resulted in diets with 5.6 and 16 g/kg DM and Ca:P ratios of 1.3 and 0.4 for the maintenance and high phosphate diets respectively. Feeding the high phosphate diet led to evidence of renal dysfunction (reduced GFR as measured by creatinine clearance; albuminuria and glucosuria), which appeared to be reversible in the cross-over design they used which had a very long washout time between periods.

Scientists at the Waltham Pet Sciences Institute designed a series of experiments with the goal of determining the no adverse effect level of phosphorus feeding^[4]. They formulated a diet that had 4.8 g phosphorus per 1000 Kcal with 3.6g per 1000 Kcal added as inorganic phosphorus (as sodium dihydrogen phosphate). This high phosphate diet had a Ca:P ratio of 0.58. The study had a parallel group design and the high phosphorus diet was compared to a relatively low phosphorus ration containing 1.2 g/1000 Kcal of phosphorus, none of which came from inorganic sources with a Ca:P ratio of 1.08. This study was stopped after 4 weeks of feeding when several cats appeared unwell. The high phosphorus diet group demonstrated an increase in serum creatinine, blood urea, a reduction in GFR (measured by plasma iohexol clearance) associated with renal imaging changes suggestive of nephrocalcinosis. Urinary albumin excretion was significantly higher in the cats fed the high phosphorus diet as were plasma FGF23 and PTH.

A second experiment reported in the same paper^[4] examined the effect of a lower level of phosphorus supplementation on kidney function over a 6 month feeding period. The control diet had a similar formulation (1.33 g/1000kcal phosphorus with no inorganic phosphate; Ca:P ratio 1.19) and the test diet had 3.6 g/1000kcal phosphorus with 2.3g provided from an inorganic source (sodium dihydrogen phosphate). In this study, the test diet was well tolerated by the majority of cats and the study ran for the scheduled 28 weeks. However, three cats from the test group were withdrawn because serum creatinine had increased above the laboratory reference interval. Overall, serum creatinine and GFR did not differ significantly between the two groups. However, FGF23 and PTH both increased relative to baseline in the cats fed the high phosphorus diet only and urine albumin was significantly higher in the cats fed the high phosphorus diet after 4 weeks of feeding and remained elevated for the remainder of the study. Furthermore, structural changes were evident on renal ultrasonography in 9 of 25 cats fed the high phosphate diet and none of the cats fed the control diet. Thus, this level of inorganic phosphorus supplementation was associated with some evidence of renal damage.

In order to characterise the acute response to feeding the diets used in the above studies, Waltham scientists undertook some acute feeding trials^[6]. Acute feeding of the diet used in the first study described above (4.8g/1000kcal phosphorus with 3.6 g/1000kcal coming from sodium hydrogen phosphate). Feeding of this diet was associated with an acute rise (over the first 6 hours) in serum phosphorus and PTH and reduction in ionised calcium. After 24 hours, serum phosphorus was below the baseline. No rise in serum FGF23 was noted in the first 6 hours after feeding. This model system was then used to test some factors that influence the bioavailability of inorganic phosphate as measured by the rise in serum phosphorus concentration immediately post-feeding. These studies

demonstrated that: (i) the organic phosphorus content of the diet had little effect; (ii) soluble phosphate supplied as sodium tripolyphosphate (STPP) was less bioavailable than that supplied as sodium dihydrogen phosphate; and a Ca:P ratio of 1.5 to 1 reduced the phosphorus bioavailability when compared to a Ca:P ratio of 0.9 to 1; (iv) inclusion of soluble phosphate at a level of 0.5 g/1000kcal did not cause a post-prandial rise in serum phosphorus.

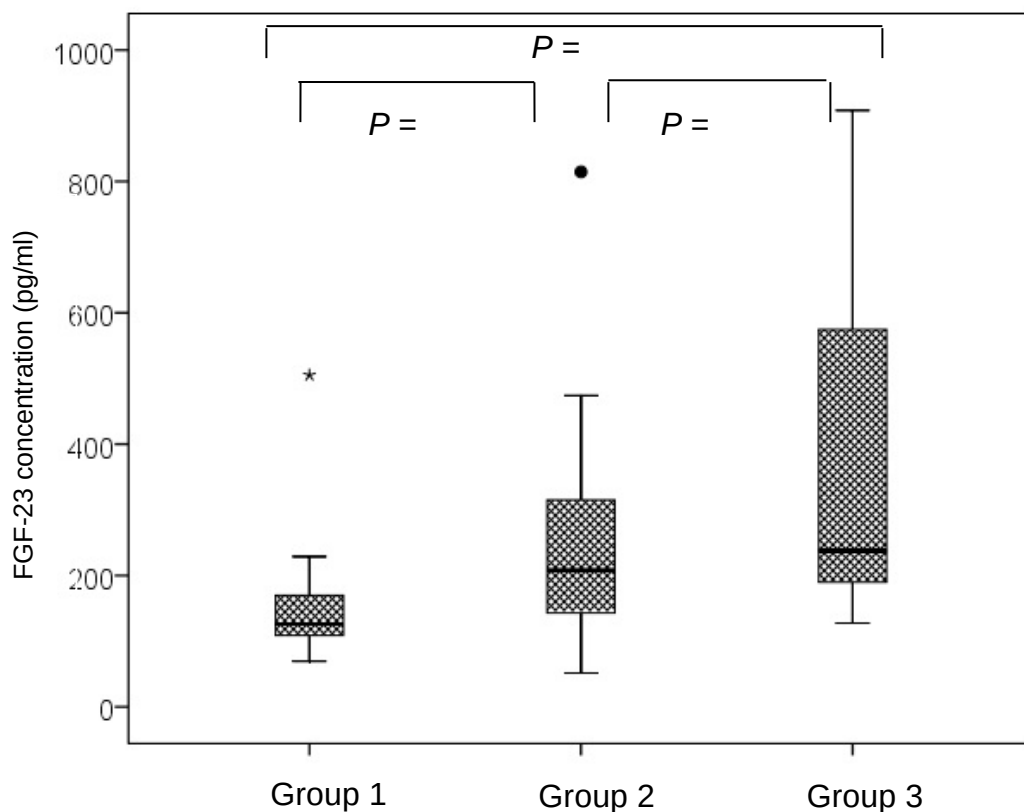
These principles were used in a long-term feeding study to determine the no observable effect level of inorganic phosphate in a formulated diet^[5]. This 30-week study had a parallel group design and consisted of 3 groups: a control group fed a diet with no added inorganic phosphorus and low total phosphorus (1.4 g/1000kcal) with a Ca:P ratio of 0.97 and two groups fed test diets each with added STPP (1 g/1000kcal) giving a total phosphorus content and Ca:P ratios of: (a) 4g/1000kcal and 1.04 (moderate diet) and (b) 5g/1000kcal and 1.27 (high phosphorus diet). Neither test diet was associated with any observable adverse health effects over the 30 week feeding period during which time kidney and bone health in particular were closely assessed. Hormonal changes associated with feeding the test diets showed that feeding the moderate phosphate diet was associated with increased production of FGF23, presumably required to ensure phosphate homeostasis was achieved over the feeding period.

The Evidence in Feline Medicine – Naturally Occurring Kidney Disease

There is little epidemiological evidence in the literature to suggest that feeding diets formulated by adding soluble sources of highly bioavailable phosphorus (such as sodium dihydrogen phosphate) is associated with development of chronic kidney disease in cats. Böswald et al (2018)^[14] conducted a retrospective study of cats presenting to their clinic where a comprehensive nutritional history allowed the composition of diets fed to be assessed. Of the 64 cats presenting to this nutritional clinic over a 6.5-year period for evaluation of CKD, it was possible to assess the phosphorus intake of 16 cases from the diet questionnaires completed. These were matched to control cases presenting to the nutritional clinics for other reasons (senior cats >8 years of age) and their phosphorus and protein intakes were compared. The cats diagnosed with CKD had significantly higher phosphorus intake when compared to the controls (170 ± 36 vs. 123 ± 34 mg P/kg BW^{0.67}; $p < .05$).

Evidence that disturbances in phosphate homeostasis precede the onset of azotaemic CKD in cats possibly support the hypothesis that whole body phosphate overload predisposes cats to the development of CKD. Finch et al., (2013)^[15] demonstrated that plasma concentrations of FGF23 predicted incident azotaemia in healthy geriatric cats. Healthy cats over the age of 9 years with plasma creatinine concentrations within the reference range were recruited to a prospective study and followed for 12 months. After 12 months, they were divided into three groups based on their kidney function at that time. Group 1 had normal kidney function, group 2 had plasma creatinine concentrations that were borderline (but within the reference range) associated with urine specific gravity below 1.035 and group 3 were persistently azotaemic. Figure 1 shows box and whisker plots of the plasma FGF23 concentrations of these three groups of cats at the initial screening time points.

Figure 1 (reproduced with permission from Finch et al., 2013 J Vet Intern Med. 2013; 27(2):227):



Clearly, cats whose kidney function remained normal over the 12-month period (Group 1) had significantly lower plasma FGF23 concentrations than those developing azotemic CKD (Group 3) at the initial screening period. At this initial health screen neither plasma phosphorus nor plasma creatinine concentrations differed between groups. This supports the view that bone mineral disturbances occur early in the course of CKD and provides the rational for the concept that feeding a phosphate restricted diet in early CKD would be beneficial. However, these observational studies do not prove a causative link between phosphate intake or the presence of bone mineral disturbance in cats prior to the onset of azotaemic CKD and the development of CKD. Prospective intervention studies are required to address this question. To date, the evidence is equivocal ^[16].

Identifying Cats at Risk of Developing Azotaemic CKD for Targeted Intervention

In order to undertake prospective intervention studies with the best chance of determining whether reducing phosphate intake is renoprotective and delays the onset of azotaemia, it would be useful to have screening tests that identifies this 'at risk' population of cats. For general practitioners undertaking annual health screens on older cats a number of tests are now available that increase the chances of identifying cats at high risk of developing azotaemic CKD within 1 to 2 years of screening. The first of these was symmetric dimethyl arginine (SDMA) a breakdown product of proteins containing methylated arginines, ubiquitous in cells throughout the body. SDMA, like creatinine, is a surrogate marker of GFR ^[17] but its production is not impacted by muscle wastage. Prospective studies in colony cats suggest it detects CKD earlier (by about 17 months) than creatinine^[18]. Serial screening of cats on an annual basis provides a means of assessing changes in biochemical parameters over time. Patterns in changes in multiple analytes related to kidney function (plasma creatinine, blood urea, urine specific gravity, urine protein to creatinine ratio and urine pH) have been assessed in large groups of cats undergoing regular health screens. Using machine learning techniques, algorithms have been developed to identify the patterns of test results that best predict cats that will develop azotaemic CKD and so be given a diagnosis of CKD within 6 to 24 months following screening ^[19,20].

Once identified as a cat at high risk of developing CKD within the next 1 to 2 years, the question practitioners often have is how does this knowledge change the way we manage these cases? Identifying the at-risk patients is just the start – determining how best to treat them and recognising they are likely to have heterogeneous underlying disease mechanisms causing renal damage and devising ways of determining which process(es) are active in a particular patient is the next step we need to develop. In the case of identifying cats that are overloaded with phosphate (which may be a factor leading to the underlying kidney disease), measurement of plasma FGF23 would be a marker that supports such a diagnosis and would strongly suggest using dietary phosphate restriction as a means of managing such a case at this stage. Recent studies at the RVC demonstrated that apparently healthy cats screened and found

to have elevated serum SDMA had significantly higher FGF23 suggesting that a proportion of these cats had significant mineral bone disturbances and may well benefit from feeding a phosphate restricted diet ^[21]. Other markers under investigation at the present time are urinary markers of tubular damage, possibly indicating ongoing active acute kidney damage, which in the CKD patient might indicate useful information could be obtained from renal biopsy that would inform treatment in such early-stage patient.

Conclusions

Knowledge of phosphate homeostasis has increased over the last 10 years and is highly relevant to both the development and progression of CKD in cats. The consumption of diets containing highly soluble inorganic salts of phosphorus exceeding 1 g/1000kcal added to the formulation to balance the diet may, if fed in a formulation that has a low Ca:P ratio (below 1), be damaging to the kidney. Prospective studies are needed to determine whether phosphate restricting cats which are at risk of becoming azotaemic and have evidence of phosphate overload (through elevated serum FGF23 concentrations) are required. Algorithms developed by machine learning techniques together with novel biomarkers (plasma and urinary) of kidney function and renal damage will assist in identifying cats at risk for further investigation and study. Tailoring specific interventions to individual cats will depend on refining our diagnostic capabilities for these early-stage cats recognising that CKD is a heterogeneous syndrome and this is the stage at which initiating causes are most likely possible to address.

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Cutting Edge Updates on Chronic Kidney Disease: Bone Mineral Disturbances – What Do We Know & Why Does it Matter?

Jonathan Elliott, MA, VetMB, PhD, DECVPT, MRCVS, FHEA

Introduction

Chronic kidney disease (CKD) is the most common cause of death in cats surviving to 5 years of age^[1]. It is a heterogeneous syndrome, which progresses at variable rates. Progression is driven by both extrinsic and intrinsic factors. Plasma phosphate at diagnosis is a factor that is associated with progression of cats with azotemic CKD (>25% increase in plasma creatinine within 12 months) both in IRIS CKD stages 2 and 3^[2]. Accumulating evidence suggests that feeding healthy cats diets that are high in phosphate, particularly where highly bioavailable inorganic phosphate has been included, is associated with kidney damage^[3] (see Lecture 1). Thus, phosphate homeostasis in general and bone mineral disturbance (BMD; formerly secondary renal hyperparathyroidism) in particular are important factors in the progression of CKD in cats and intervention measures that address BMD are currently a mainstay in the management of feline CKD.

Disturbances of Phosphate Homeostasis in Feline CKD

Research in the 1980s demonstrated that cats fed high levels of phosphate when renal mass had been surgically reduced developed renal lesions in the remnant kidney (fibrosis and mineralisation in particular)^[4]. This study clearly demonstrated that high dietary phosphate intake (1.56% DM) led to more marked pathology in the remnant kidney in terms of interstitial fibrosis, inflammation and mineralisation after 12 months of feeding when compared to cats fed a phosphate restricted diet (0.24% DM). Interestingly, over this 12-month period, no progressive decrease in renal function following model establishment was seen in this 11/12 nephrectomy model.

Naturally occurring CKD in cats leads to increased circulating levels of PTH^[5], particularly marked in the later stages (Uraemic and End stage were similar to IRIS CKD Stages 3 and 4). Plasma PTH reduced in response to feeding of a commercial phosphate restricted renal diet^[6]. Whilst plasma phosphate concentrations stabilised within 4 to 8 weeks of initiating feeding of this diet, plasma PTH concentrations continued to decrease over 4 to 5 months. Cats that continued eating their standard maintenance diet tended to have increasing PTH concentrations over the same period. Cats with IRIS stage 2 and 3 CKD fed a commercial renal diet +/- a phosphate binder (aluminium hydroxide) with the aim of controlling PTH, survive for longer^[7]. This study was not randomised and the cats were all offered renal diet at entry to the study. Those whose owners were able to feed the renal diet tended to live longer than those whose owners were unable to transition their cats onto the diet. At entry to the study the two groups of cats (29 that ate the clinical diet and 21 that were maintained on their standard maintenance diets) did not differ significantly in terms of age, renal function, blood pressure or any other factors that predict outcome. Nevertheless, the study design was not optimal to determine the feeding of the diet as the cause of improved survival.

A second study, employing a different commercially available clinical renal diet (also phosphate restricted), showed that cats with IRIS CKD stages 2 and 3 had fewer uremic crises and renal deaths when randomised to receive the commercial renal diet^[8]. This confirms the benefit of feeding cats with established CKD a high quality phosphate restricted diet with a prospective randomised controlled clinical trial (i.e. level 1 evidence). In both these studies^[7,8], the commercial clinical renal diets differed from standard maintenance diets in several respects (restricted in protein, phosphorus, sodium and supplemented with potassium, n3-polyunsaturated fatty acids and B vitamins). These early studies showed that secondary renal hyperparathyroidism is common in the later stages of CKD and that dietary phosphate restriction (+ or – intestinal phosphate binders) reduced serum PTH and phosphate and improved survival.

Phosphate, however, is predominantly an intracellular anion. It seems likely that measurement of serum phosphorus is like looking at the tip of the iceberg and that accumulation of phosphate occurs long before plasma phosphate and PTH increase. Some evidence that this was the case came from unpublished observations from Barber et al., (1999) and Elliott et al., (2000)^[6,7] that whilst plasma phosphate reduced and stabilised in cats with CKD within the first 2 to 3 months of feeding a clinical renal diet whereas plasma PTH could continue to decrease for up to 12 months. Conversely, if the owner decided to feed a standard maintenance diet again, interestingly, PTH increased before plasma phosphate did. Furthermore, it was clear that some cats in CKD stages 2 to 3 had relatively normal plasma phosphate and PTH concentrations (>50% of the stage 2 CKD cats had normal plasma PTH concentrations and an even higher proportion had within reference interval plasma phosphate concentrations). However, the benefit of dietary phosphate restriction seemed to apply across the whole group of cats fed the phosphate-restricted diets.

CKD New Understanding of Phosphate Homeostasis in CKD

The discovery of FGF23 has given us the tool to assess disturbed phosphate homeostasis long before plasma phosphate or PTH increase. As glomerular filtration rate (GFR) falls, if dietary phosphate intake remains the same, the rate of phosphate excretion reduces (as phosphate excretion is dependent on GFR). Thus, if plasma phosphate does not increase, phosphate in another body compartment (such as intracellular fluid or bound stores) must increase. Studies in the last decade at the Royal Veterinary College have suggested this to be the case.

Finch et al., (2013)^[9] demonstrated that plasma concentrations of FGF23 predicted incident azotaemia in healthy geriatric cats (see lecture 1). This supports the view that bone mineral disturbances occur early in the course of CKD and provides the rationale for the concept that feeding a phosphate restricted diet in early CKD would be beneficial. However, prospective intervention studies are required to address this question.

Clinical use of FGF23 to determine which cats would benefit from dietary phosphate restriction most is hampered by the lack of a commercial test for this hormone and so its study is confined to the research setting. In a retrospective cross-sectional study of cats with azotaemic CKD, plasma FGF23 concentrations showed a graded increase with stage, with statistically significant difference being evident between all stages^[10]. This contrasts with plasma PTH concentration, which showed much more heterogeneity within a stage with far greater overlap between stages^[10]. Furthermore, within a stage, if the serum phosphorus concentration was within the target range for that stage (IRIS CKD stage 2: ≤ 4.5 mg/dl; IRIS CKD stage 3: ≤ 5.0 mg/dl) the FGF23 concentration was significantly lower when compared to cats within that stage where the serum phosphorus concentration was above the target for that stage. Plasma creatinine concentrations were not different between these sub-groups of cats within a particular stage suggesting that plasma FGF23 concentrations were indicative of phosphate overload within a given stage.

Another retrospective longitudinal study involving 33 cats that had been successfully transferred onto a clinical renal diet, demonstrated the changes in circulating FGF23 and PTH over a two month period in response to the diet^[11]. Cats ($n=15$) that had high serum phosphorus concentrations for their stage showed significant reductions in serum phosphorus, PTH and FGF23 after two months of consuming the diet. However, those with serum phosphorus concentrations within the IRIS target range for their stage at diagnosis showed no change in serum phosphorus or PTH after two months of dietary therapy but did show a significant reduction in serum FGF23 levels, demonstrating a beneficial effect of feeding a phosphate restricted diet to these cats. The retrospective nature of this study is a significant limitation as there was not true control group (where no dietary intervention was applied) for comparison. The authors did include data collected contemporaneously from cats not receiving a diet change over a similar period to demonstrate that there was no change in FGF23 concentrations in these cats over time. These data suggest that serum FGF23 could be used as a sensitive marker of whole body phosphate in cats with CKD and is probably the most sensitive marker of the response to dietary phosphate restriction once the serum phosphorus concentration is within the IRIS target range.

As a circulating marker FGF23 also shows great promise as a prognostic indicator predicting all-cause mortality and progression^[12]. In this retrospective study involving 214 cats diagnosed with CKD, factors associated with all-cause mortality (using Cox regression) were assessed. Survival was negatively and independently associated with plasma creatinine ($P = .002$) and FGF-23 concentrations ($P = .014$), urine protein-to-creatinine ratio ($P < .001$) and age ($P < .001$). Survival was positively associated with PCV ($P = .004$). One hundred and five cats had long enough follow-up to assess whether progression occurred. Progression defined as a 25% increase in plasma creatinine concentration within 12 months of diagnosis; using logistic regression. Only age and plasma logFGF23 concentration were independent predictors of progression of CKD in the multivariate logistic regression analysis. Neither plasma phosphorus nor PTH concentrations made it into the multivariate model as independent factors supporting the contention that plasma FGF23 concentrations are the best measure of the severity of BMD in cats with CKD.

When Does the FGF23-PTH System Become Maladaptive?

From the above discussion and from what we know of the function of FGF23 in the early stages of CKD it is helpful in enabling cats with falling GFRs to maintain phosphate homeostasis and excrete an appropriate amount of phosphorus each day to remain in balance. The stimulus leading to secretion of FGF23 from bone is poorly characterised but seems to relate to total body phosphate load. Its effects reduce phosphate entry into extracellular fluid through the gut (by inhibiting calcitriol synthesis) and from bone (by inhibiting PTH synthesis and secretion). As kidney disease progresses the ability of the kidney to make α -klotho, the co-factor needed for FGF23 to activate its receptors to bring about its physiological effects is reduced. Klotho-deficiency is thought to occur at the point at which FGF23's effects become maladaptive and its production from bone increases well beyond that required for its physiological functions described above. At this point in the pathophysiology of BMD in CKD, circulating PTH concentrations increase as the ability of FGF23 to suppress PTH secretion is lost. In human medicine, low circulating levels of α -klotho and high circulating levels of FGF23 herald progression of CKD and a poor prognosis^[13].

The pathological effects of FGF23 in the absence of α -Klotho are controversial but have been proposed to include fibrosis, endothelial cell dysfunction, vascular mineralisation and cardiac muscle hypertrophy^[14]. The relevance of these effects to feline medicine remain to be determined. Initial studies have demonstrated reduced expression of α -klotho in the kidney of cats with increasing severity of CKD (as defined by IRIS staging)^[15]. However, no reductions in circulating concentrations of soluble α -klotho have been found as IRIS stage of CKD increases in cats^[16]. Further studies are necessary to characterise and understand the FGF23- α -klotho axis in the cat.

Is Dietary Phosphate Restriction Appropriate for All Cats With CKD?

From the above discussion, it would seem that the application of dietary phosphate restriction, such as is delivered by clinical diets formulated for kidney disease, would be appropriate for all stages of CKD. However, it is well recognised that some cats with CKD develop hypercalcaemia^[17]. Whilst lowering plasma phosphate concentration would appear to be beneficial in the face of hypercalcaemia, reducing the risk of soft tissue mineralisation, sometimes hypercalcaemia appears to be triggered by feeding a clinical renal diet^[6,18]. Phosphate restricted clinical renal diets tend to have higher Ca:P ratios than standard grocery diets (as a result of phosphate restriction). In some cases, reducing the degree of phosphate restriction leads to a reduction in serum calcium without compromising the control of bone mineral disturbance^[18].

Prospective studies are required to determine how cats that become hypercalcaemic when fed a clinical renal diet can best be identified and to understand the optimum dietary management of these cats. Rather than feeding the standard clinical renal diet with a high Ca:P 1.9:1 due to a highly restricted level of phosphorus (typically 0.8 g/1000kcal), feeding a less phosphate-restricted ration with a lower Ca:P ratio appears to provide effective management of BMD without giving rise to ionised hypercalcaemia. Some cats present with ionised hypercalcaemia at diagnosis of CKD. The optimal management of cats with hypercalcaemia secondary to CKD, whether diet-induced or otherwise remains to be determined and requires further studies to understand the under-lying pathophysiological mechanism(s) involved. These observations suggest measurement of blood ionised calcium at diagnosis of CKD and following instigation of dietary therapy would be advisable to tailor the treatment approach to the individual patient. Furthermore, this highlights the fact that the approach of applying a standard dietary approach to all cats diagnosed with CKD is too simplistic and tailoring dietary therapy to the needs of the individual patient is more appropriate.

Why is Whole Body Phosphate Overload Detrimental to the CKD Patient? Why Do We Need to Consider Serum Magnesium Concentration?

In human medicine, the most common cause of death in CKD patients that are on dialysis is cardiovascular disease, which is thought to occur secondary to vascular mineralisation^[19]. Radiographic evidence shows that this occurs in cats with IRIS CKD Stage 4. *In vitro* data demonstrate that exposure of vascular smooth muscle cells to media containing phosphate of 2 mmol/l (6.2 mg/dl) changes the phenotype of these cells so that they secrete extracellular matrix which then becomes mineralised^[20]. Magnesium is an antagonist of this process *in vitro*. This literature stimulated our group to examine serum magnesium concentrations in cats with CKD to determine whether BMD is influenced by serum magnesium, an analyte hitherto ignored in feline practice.

Low serum magnesium concentrations in cats with CKD are associated with increased FGF23 concentrations (independent of plasma phosphate)^[21]. There is an interaction between serum phosphate and magnesium in predicting progression of CKD. Whether correcting the low serum magnesium improves the outcome of hypomagnesemic cats with CKD remains to be determined. Cats with serum magnesium below 0.8 mmol/l (1.9 mg/dl) should definitely be monitored closely and attention should be paid to controlling plasma phosphate to mitigate the bone mineral disturbances as good control of this complication of CKD is associated with favourable outcomes^[7]. It seems likely that the negative impact of low serum magnesium concentration is related to magnesium's role as an inhibitor of vascular and possibly other soft tissue mineralisation. FGF23 when produced in excess likely promotes vascular calcification. Exactly how this relates to progressive kidney pathology remains to be determined. Measurement of physiologically active soluble klotho and calciprotein particles and other inhibitors of vascular calcification, such as Fetuin A may provide further insight into the different phases of BMD associated with CKD in the cat.

Conclusions

Bone mineral disturbance is an important, early and progressive consequence of feline CKD. A greater understanding of the physiology of phosphate homeostasis in the cat and the factors influencing BMD pathophysiology in individual cats will, in the future, assist in veterinarians tailoring the management of CKD to the individual patient at all stages. Recognition and understanding of the point at which adaptive mechanisms designed physiologically to enhance renal excretion of phosphate, become maladaptive and lead to osteodystrophy and vascular (and other soft tissue) mineralisation would assist in the management of this important syndrome associated with CKD.

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Learning the Ins & Outs of Taking Feline Blood Pressure Without Elevating Yours

Ellen Carozza, LVT & Kelly A. St. Denis, MSc, DVM, DABVP (Feline)

Do you regularly monitor your feline patients' blood pressures? Have you wondered if maybe you should and if so, how? Do you wonder about how the stress of a veterinary visit affects a cat's blood pressure or what would be the best way to take blood pressure readings from a cat that you can depend on? Join feline specialist Dr. Kelly St. Denis and Cat Friendly Certified, LVT, Ellen Carozza for a practical approach to blood pressure in cats.

Learning Objectives

- Gain insight into the physiological factors that impact blood pressure and the most common causes of hypertension in cats
- Understand the difference between Dopplers, traditional oscillometric and high definition oscillometric devices
- Become comfortable with using blood pressure monitoring devices including the 'dos and dont's'
- Learn how to apply your Cat Friendly handling skills for blood pressure measurements

Causes & Effect:

Systemic hypertension is a common medical problem in the feline species that is often missed during routine visits ¹. Feline systolic blood pressure (SBP) increases with age ², thus increasing the risk for systemic hypertension ³. Hypertension can be divided into three categories. Primary or idiopathic hypertension occurs where no underlying disease is present. Idiopathic hypertension occurs in 13-20% of cases. Secondary hypertension is that in which an underlying disease is present which is directly causing or predisposing to hypertension. Lastly, situational hypertension(aka white coat hypertension) is a real and documented phenomenon in the feline species. ⁴

Secondary Hypertension

Chronic Kidney Disease is commonly associated with hypertension, with 19-65% of cats with CKD developing hypertension at some time. The reverse is also true, in that unrelated hypertension can predispose to azotemia as a result of elevated systemic blood pressures and their impact on the glomerular filtration rate (GFR). Azotemia may be found in up to 74% of hypertensive cats. As a secondary cause of hypertension, hyperthyroidism is also common. Ten to 23% of hyperthyroid cats may be found to be hypertensive at the time of diagnosis with hyperthyroidism. Once euthyroid, 25% of normotensive, hyperthyroid cats may develop hypertension. Primary hyperaldosteronism (PHA) occurs as a result of excess aldosterone production independent of its regulator, angiotensin II. Forty to 60% of cats with PHA are hypertensive. Other less common secondary causes of hypertension include diabetes mellitus, pheochromocytomas, and pituitary hyperadrenocorticism.

Situational Hypertension

Stress and anxiety can impact systemic blood pressure in the feline species. Stresses associated with the trip to the clinic, handling by staff, and cuff placement and inflation, can all contribute to temporary elevations in SBP. In a 1999 study evaluating the white coat effect on SBP in cats, the magnitude of the white-coat effect tended to decrease during the office visit but did not disappear. Interestingly, the mean increase in SBP was found to be significantly greater in cats with renal insufficiency. White coat (situational) hypertension is recognizable, avoidable and/or can be overcome when one approaches blood pressure measurements following the guidelines of Feline Friendly[®] practice. ⁵

Clinical signs of Hypertension

As is often the case with humans, the clinical signs of hypertension often go unnoticed in the feline species. This is further compounded by the fact that cats are masters at hiding illness. Clients often miss the subtle, early signs of sickness in their pet cats, and hypertension is no exception. Clinical signs identifiable in practice are often associated with damage or changes to those organs most sensitive to hypertension. These are referred to as target organs. Target organ damage (TOD) is identifiable in the retinas, the heart, the brain and the kidneys.

Retinas ✚ 50% of hypertensive cats can develop retinal changes (sBP>160) ✚ Tortuosity of retinal blood vessels ✚ Hemorrhage of retinal blood vessels ✚ Cotton wool patches- detachment of retina ✚ Vitreal hemorrhage	Heart ✚ Increased systemic vascular resistance can increase left ventricular (LV) wall stress which may result in concentric LV hypertrophy ✚ Gallop sounds, possibly murmurs, arrhythmias ✚ Rare sequelae: heart failure, aortic dissections
Kidneys ✚ External elevations in SBP can impact internal pressures leading to glomerular hypertension and damage ✚ Azotemia occurs in up to 74% of hypertensive cats ✚ Kidneys impact blood volume and BP through pressure natriuresis and RAAS ✚ 19-65% of cats with CKD will develop hypertension at some time	Brain ✚ Neurological signs in 15-46% of hypertensive cats ✚ Disorientation, seizures, ataxia, depression and vestibular signs ✚ Many differential diagnoses ✚ Presumptive diagnosis: signs improve with treatment

Candidates for Monitoring and Screening

The most common need for systemic BP assessment is in cats 7 years of age or over. Since blood pressures increase with age and ageing cats are at increased risk of developing hypertension, this should be regarded as *the* high-risk group requiring routine, biannual SBP monitoring. At the same time, this group should be assessed for TOD. Cats with evidence of TOD, including blindness, and patients with diseases associated with 2° hypertension will also need SBP assessment. All cats under anesthesia should be subjected to continuous SBP monitoring. Once a cat is diagnosed with hypertension, ongoing SBP monitoring is necessary.

What You Need: Scientific Equipment

Gold standard assessment of BP includes direct methods by central catheter or radiotelemetric implant. Direct methods are impractical and invasive in routine practice. Indirect methods utilizing the Doppler or oscillometric (traditional or high definition) are readily available to clinicians. Indirect methods are practical and non-invasive, but can be highly inaccurate. For this reason, knowledge of the machine, development of a standardized protocol and assessment by a limited number of trained staff is critical.⁶ Interpretation of the results based on the patient status, patient stress level and evidence of TOD is also critical.

The 'How' Makes All the Difference: Using the Equipment Right

The following should not be overlooked:

Cuff Selection

- ✓ 40% circumference of limb OR follow manufacturer's guidelines printed onto cuffs
- ✓ Snug fit

Cuff Placement

- ✓ Forelimb, tail, hind limb
- ✓ The inflation tube *must* be placed over the artery
- ✓ The inflation tube must be placed in a direction away from (not toward) the patient
- ✓ The cuff position is ideally in the same horizontal plane as the heart

Standardized Protocol

- ✓ Acquire a minimum of 6 readings of the SBP

- ✓ Drop first reading as it will often be unreliable in the cat
- ✓ Average remaining readings
- ✓ Only experienced individuals should be assigned the task of obtaining blood pressure readings

What You Need: Feline Friendly Environment

Choosing the Right Setting

Every patient will be unique the setting that calms them best. It is important to explore the following options with each patient and determine what is best for *that* patient. Record it in their record in a prominent location for future use.

- ✓ In carrier (lid on/lid off)/out of carrier
- ✓ Exam room vs. Treatment vs. ICU
- ✓ WARM, QUIET, DIMMED environment
- ✓ Warm soft blankets previously sprayed with Feliway
- ✓ Minimize individuals present: with or without client, experienced personnel, cat friendly personnel, ask other staff not to walk through area

Analgesics

- ✓ Most analgesics will alter SBP
- ✓ Many cats >7 have DJD and other sources of chronic pain
- ✓ Minimize handling during SBP readings
- ✓ Consider low dose gabapentin 6-10 mg/kg prior to the visit. The impact of gabapentin on SBP is currently unknown, although it is perceived to be minimal. Studies are pending.

Establishing Criteria for Therapeutic Decision Making

Before determining if a cat is truly hypertensive, the clinician must be sure of having measured the SBP carefully according to the following:

- Measure SBP according to feline friendly practice protocols
- Measure SBP according to manufacturer directions
- Measure SBP according to a standardized protocol

According to the panel for the ISFM Consensus Guidelines on the Diagnosis and Management of Hypertension in Cats ¹, the diagnosis of hypertension can be made in the four distinct circumstances. A single occasion is defined as one visit obtaining a series of readings based on the standardized protocol.

Diagnosis of Feline Hypertension	
	Indirect SBP is ≥ 150 mmHg on a single occasion, <i>and</i> there is clear evidence of ocular or neurological TOD. Note: if clinical signs do not respond appropriately to adequate antihypertensive therapy, the diagnosis should be re-assessed and other potential causes of the signs investigated.
	Indirect SBP is ≥ 160 mmHg on at least two separate occasions, <i>and</i> there is evidence of TOD including ocular, neurological, cardiac or kidney damage.
	Indirect SBP is ≥ 170 mmHg on at least two separate occasions, <i>and</i> the clinician does not consider 'white coat hypertension' is likely to be the cause.
	Indirect SBP is < 150 mmHg, but there is <i>clear</i> evidence of active ocular TOD. Note: cats should be monitored carefully. If there is any doubt about the diagnosis of hypertension, the need for long-term therapy should be reassessed by trial withdrawal of therapy once stable, and monitoring of BP and clinical signs.

Therapies and Therapeutic Targets

1. Amlodipine besylate (Calcium channel blocker): This is a potent peripheral arterial dilator and is the **drug of choice in feline systemic hypertension**. **DOSAGE: 0.625-1.25 mg/cat PO q24 or DOSAGE: 0.125-0.25 mg/kg PO q24h**. Reassess SBP in 3-5 days the maximum amlodipine recommended dosage is 2.5 mg/cat q24h.
2. Telmisartan (Angiotensin receptor blocker (ARB)): This agent is effective in controlling systemic hypertension at high doses. It is now licensed for use in the U.S. as a primary anti-hypertensive. **DOSAGE: 1.5 mg/kg PO q12h 14d then 2.0 mg/kg PO q24h long term^{7,8}**. Telmisartan may be beneficial as an adjunct to refractory treatment with amlodipine. **DOSAGE: 1.0 mg/kg PO q24h**
3. Benazepril (ACE inhibitor): This agent is not effective alone in the control of systemic hypertension, but may be beneficial as an adjunct to refractory treatment with amlodipine. The medication should not be added if the patient is dehydrated. **DOSAGE: 0.5-1.0 mg/kg PO q24h**
4. Atenolol (β -blocker) tachycardia, hyperthyroidism **DOSAGE: 1.0-2.0 mg/kg PO q12h**
5. Propranolol: (β -blocker)
6. Enalapril: (ACE inhibitor)
7. Ramipril: (ACE inhibitor)
8. Spironolactone: Indicated in cases of hyperaldosteronism

Therapeutic Goals

The therapeutic goals in the management of feline hypertension are simple. Prescribed medications should effectively control SBP with the goal of decrease TOD. In cases of secondary hypertension, identified primary diseases should be treated, controlled and/or cured.

Key Points

1. Hypertension is a well-recognized but under-diagnosed condition in cats
2. Routine screening and monitoring is key
3. Veterinary technicians play an indispensable role in developing standards of care for feline friendly blood pressure monitoring

For more information, visit the AAFP's Feline Hypertension Educational Toolkit at www.catvets.com/hypertension.

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Spring into Feline Medicine



THREE-DAY **VIRTUAL LIVE CE EVENT**

Sunday, April 18th | Wednesday, April 28th | Saturday, May 8th

ALL TIMES ARE EASTERN TIME ZONE

Sunday, April 18, 2021

TIME	SESSION TITLE	SPEAKER	SPONSOR
12:00 - 1:20 pm	Top Tips for Management of Stress-associated Conditions in Cats	Dr. Christopher Pachel	
1:40 - 2:40 pm	Feline Behavior: More Than Just a Naughty Cat	Dr. Christopher Pachel	
2:50 - 3:50 pm	Feline Hypersensitivity Dermatitis: Understanding Cause & Therapy	Dr. Michael A. Rossi	
4:00 - 5:00 pm	Role of Probiotics in the Management of Diarrhea in Cats	Dr. Michael Lappin	

Wednesday, April 28, 2021

TIME	SESSION TITLE	SPEAKER	SPONSOR
12:00 - 1:20 pm	Peak Cat Care: Getting the Most from your Feline Exam	Dr. Elizabeth Colleran & Dr. Margaret Gruen	
1:40 - 2:40 pm	Cutting Edge Updates on Chronic Kidney Disease: Understanding Dietary Phosphorus & Renal Health	Dr. Jonathan Elliott	
2:50 - 3:50 pm	Cutting Edge Updates on Chronic Kidney Disease: Bone Mineral Disturbances – What Do We Know & Why Does it Matter?	Dr. Jonathan Elliott	
4:00 - 5:00 pm	Learning the Ins & Outs of Taking Feline Blood Pressure Without Elevating Yours	Ms. Ellen Carozza & Dr. Kelly St. Denis	

Saturday, May 8, 2021

TIME	SESSION TITLE	SPEAKER	SPONSOR
12:00 - 1:20 pm	Keeping Felines Feisty Despite Frailty	Dr. Shelia Robertson & Dr. Bonnie Wright	
1:40 - 2:40 pm	Nutritional Myths: Cat Owner Questions & Concerns	Dr. Julie Churchill	
2:50 - 3:50 pm	Complicated Endocrine Cases	Dr. Cynthia Ward	
4:00 - 5:00 pm	Secrets to Managing Today's Diabetic	Dr. Cynthia Ward	

Keeping Felines Feisty Despite Frailty

Sheilah Robertson, BVMS (Hons), PhD, DACVAA, DECVAA, DACAW, DECAWBM (WSEL)
& Bonnie Wright, DVM, DACVAA

Introduction

Aging cats are an increasing demographic, similar to the so called “silver tsunami” in human medicine. Frailty is a syndrome, often associated with advancing age and is commonly seen in cats. A decrease in functional reserve of vital organs, sarcopenia and dysregulation of the immune system leads to a decline in health and cognition, resulting in medical and physical vulnerability. With the increasing awareness of the scope of issues faced by the aging feline and the increasing skill, knowledge and gerontological care that can be provided by veterinarians, it is critical for everyone who sees cats in their clinic to understand how to support these patients and their owners.

A more thorough and exhaustive review of this subject is available in the 2021 AAFP Senior Care Guidelines.

Relationships

The cat caretaker is a critical member of the medical care team. They are vital for assessing pain, wellbeing, and Quality of Life (QoL), and for providing medical and nursing care. Owner education is thus paramount, and the growing number of tools, such as AAFP initiatives, available to help them on their journey is timely. What constitutes QoL for their cat, understanding caregiver burden, anticipatory grief, and the toll that polypharmacy may have on the owner-cat relationship are all important topics that require in depth conversations between the veterinarian and owner. These can be difficult conversations, and like specialist human physicians, we should educate ourselves on how to guide these discussions and keep them patient centric.¹ We must also remember there are several budgets to consider during these conversations which include financial, time, emotional and physical.

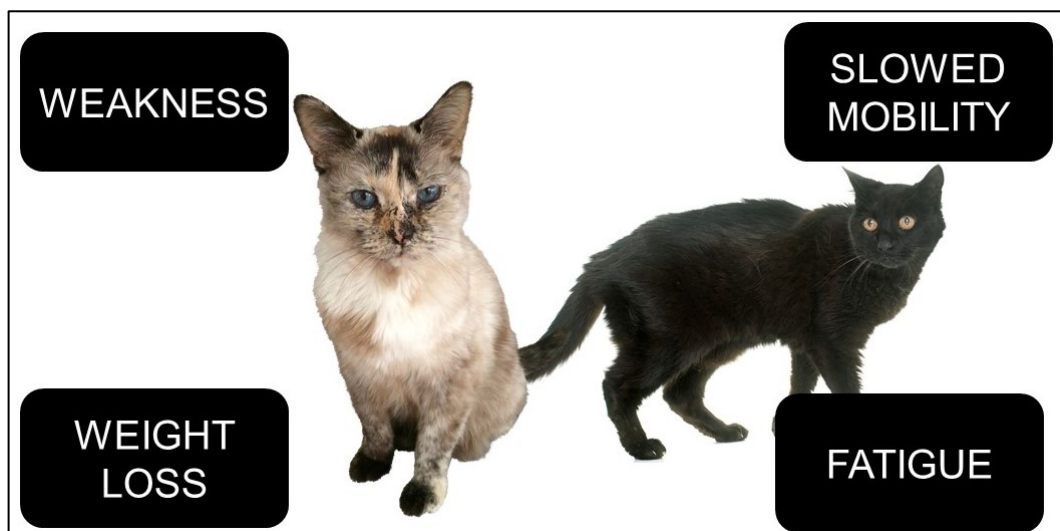
The Physical Exam

Longer appointment times, and the value of cat-only facilities and feline friendly handling practices cannot be over-emphasized. In addition to a thorough musculoskeletal, dental, and medical exam, learning myofascial palpation skills can be transformational for diagnosing the relationship between pain and somatic/visceral disease. A myofascial exam is helpful to assess the viscosity, mobility, temperature, and comfort of soft tissue structures. If performed correctly, the exam is a soothing, gentle, and inquisitive approach for assessing pain from multiple sources, including the appendicular and axial and skeleton, soft tissue and viscera.

Age and frailty

Aging and frailty do not always go hand in hand. Categorizing cats (or people) as adult, senior or geriatric is based on where they are in an expected lifespan. Frailty on the other hand is a medical diagnosis or designation. It comprises several key factors as shown in **Figure 1**.

Figure 1. The components of frailty



Identifying Comorbid Conditions

- Unexplained trends in weight (up or down), body condition score, muscle condition score and behavioral signs suggestive of pain should be investigated and managed as diseases.
- Hypertension is common in aging cats and can be associated with several disease states.
 - *Videos produced by ISFM are available at jfms.com and <https://www.youtube.com/user/iCatCare>.*
- Hydration status can be affected by chronic kidney disease, dental disease, and diabetes mellitus
- Thyroid disease
- Cardiac disease
- Dental disease
- Gastro-intestinal disease
- Neoplasia

Complex Disease Treatment Concepts

Integrative care includes both pharmaceutical and non-pharmaceutical approaches to feline care. Supporting owners includes teaching them techniques to increase exercise and play, use creative feeding strategies and food puzzles, techniques for on soft tissue such as mobilizing forms of massage. These are relationship builders for the veterinary care team, owner, and patient. Adding more and more medications often takes a toll on relationships and ultimately result in non-compliance and often owner aversion by the patient – there is nothing more heartbreaking than having a cat run away and hide, or become defensive, because it is medication time.

Adaptive and Maladaptive Pain

Adaptive pain includes nociceptive and inflammatory pain. Nociceptive pain is an “early warning” or protective mechanism; it may or may not result in tissue damage but is essential for survival. It is typically easy to identify the cause of adaptive pain and normally it is reversible or self-limiting if treated appropriately.

Maladaptive pain is not protective, it has no biological value, but is the cause of great suffering in humans and animals and should be considered a disease in itself. It results from changes in pain processing systems and can be separated into two types:

1. *Neuropathic pain*; this is a result of neural tissue damage, central or peripheral.
2. *Functional pain*; no neural damage or inflammation can be detected, but the driving force for pain is a malfunction or dysfunction in the nociceptive system.

In maladaptive pain there is amplification and facilitation of what can be thought of as “pain traffic” and increased sensitivity to stimuli. Other things that contribute to maladaptive pain are an imbalance between inhibitory and excitatory nociceptive input, altered descending inhibition, decreased activation of endogenous analgesic systems and spontaneous ectopic discharge from injured nerves. The separation between adaptive and maladaptive pain is not always clear cut and several painful long-term conditions in cats have an inflammatory component.

Another term that is important to the concept of maladaptive pain is *central plasticity* (also called central sensitization) which is initiated through cellular wind-up. *Wind-up* is defined as a neuron’s increased response and output following identical, repeated stimuli. The term central plasticity refers to an autonomous global response that continues after the stimulus stops, or which is sustained by low level nociceptor input in the periphery.² Because some processing systems are down-regulated the term central plasticity is more descriptive than central sensitization. The result of these changes is hyperalgesia (increased pain from a stimulus that normally provokes pain) or allodynia (pain resulting from a stimulus that would not normally provoke pain), and expansion of the receptive field of neurons. Based on quantitative sensory testing studies, central plasticity is a feature of feline osteoarthritis(OA).³ For an excellent review of maladaptive pain see the article by Adrian *et al.*⁴

We should think of maladaptive pain as a disease and manage it as such. After a thorough physical examination, knowing the cat’s history, and reviewing the medical records it should be possible to diagnose the type of pain they have; in this population, it is likely to be a combination of inflammatory and neuropathic pain. This allows us to move from symptom control toward mechanism-specific management as Woolf proposed.⁵ Compliance or adherence to a prescribed treatment can fail in cats because of the difficulty with medicating them and this should be one of the first things to consider when developing new treatments. One approach has been the development of feline specific anti-Nerve Growth Factor monoclonal antibodies which are administered subcutaneously every 4 to 6 weeks to alleviate OA related pain.⁶

Improving activity and mobility using appropriate analgesics, which may include joint blocks, physical activity, combined with physical medicine approaches such as acupuncture can benefit multiple diseases.

Modification of the Home Environment

Cats with impaired mobility and / or weakness will need assistance with some of their “every day” activities. These include but are not limited to:

- Accessing elevated places – use steps, chairs, and boxes to make this easier
- Eating and drinking – elevate food and water bowls
- Using a litter-box – ensure this is “easy entry” with a low access point
- Doing their “favorite thing” – this will be different for each cat
- Grooming – owners can assist with this

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Nutritional Myths: Cat Owner Questions & Concerns

Julie Churchill, DVM, PhD DACVN

Introduction

Making decisions about what to feed cats has become even more complicated for pet parents whose goal is to feed *the* best food. Cat owners have many questions about pet foods. Advice and information recommending *the* best food is readily available almost anywhere, from pet food retailers, magazines, internet sources and social media. However, these voices can be strongly biased and may compete with the veterinarian healthcare team's advice. This talk will clarify common questions cat owners have about petfood.

How to Decipher Information About a Pet Food to Make a Diet Recommendation

There is no single 'best' food for all pets since optimal nutrition depends on several things such as life stage, body condition, appetite, activity (or sedentary lifestyle), environment, and health status. Without guidance otherwise, it's common for pet parents to make decisions based on the marketing claims rather than objective nutritional information, which can be elusive or confusing. The most important source for questions about the best food for your pet, is the veterinary healthcare team, who knows the health and life stage needs of your specific pet, and can tailor the recommendation to that pet's individual nutritional needs. The veterinary team can answer questions or help find information, as well as help a pet owner make sound nutritional decisions for their pet.

Although there are significant limitations to evaluating a pet food, the label is a good place to start. Many pet owners make their choices based on label information and yet they have many questions about what they read on the pet food label. All pet food labels are required to include the following 9 items:

1. Product Name, food type
2. Net weight
3. Nutritional statement (adequacy claim or 'AAFCO' statement)
4. Basis of nutrition claim; lifestage
5. Ingredient list
6. Guaranteed analysis (% nutrient content as fed)
7. Feeding directions
8. Manufacturer or distributor name and address
9. Universal product code

A systematic approach to evaluating labels is a useful first step in assessing a product for a pet. Of all of these, the two most useful pieces of information on a pet food label are 1) the manufacturer and 2) the nutritional adequacy statement.

What follows is a suggested approach to reading labels and pet food products for indicators of a product's nutritional value and potential impact on pet health.

Suggested in descending order of importance:

The Manufacturer Information

The manufacturer's name and contact information should be provided. Contact the manufacturer whenever you have questions about a product. This can provide you with valuable information as well as an indication of how willing a company is to answer nutrition questions when contacted. The American Animal Hospital Association (AAHA) (Baldwin 2010) and the World Small Animal Veterinary Association (WSAVA, 2011) [Nutritional Assessment Guidelines](#) includes an excellent list of questions or considerations to ask of manufacturers.

- The manufacturer should employ at least one full-time qualified nutritionist. Appropriate qualifications are a PhD in animal nutrition or board certification by the American College of Veterinary Nutrition or European College of Veterinary Comparative Nutrition.
- The manufacturer should test its diets with AAFCO (the Association of American Feed Control Officials) feeding trials. If AAFCO feeding trials are not conducted, the manufacturer should, at a minimum, ensure that diets meet AAFCO nutrient profiles through analysis of the finished product.
- The pet food company should own the manufacturing plant or plants where the food is manufactured.
- The manufacturer should practice strict quality-control measures. Examples include certification of a manufacturer's procedures (eg, Global Food Safety Initiative, Hazard Analysis and Critical Control Points, or American Feeding Industry Association); testing ingredients and end-products for nutrient content, pathogens, and aflatoxins; materials risk assessments; and supplier audits.

- The manufacturer should be able to provide a complete nutrient analysis for any pet food of interest (not only the guaranteed analysis, which is listed on the label, but the average [typical] analysis as well). The manufacturer should be able to provide exact values for all nutrients. This should ideally be provided on an energy basis (ie, grams per 100 kilocalories or grams per 1,000 kilocalories), rather than on an as-fed or dry-matter basis, which does not account for the variation in energy density among foods.
- The manufacturer should be able to provide the number of calories for any food on any requested weight or volume basis (eg, per gram, per pound, per cup, or per liter).
- The manufacturer should conduct and publish research in peer-reviewed journals.

Additionally, this author values manufacturers who do not use negative advertising or fear-based misinformation in their advertising or website.

Nutritional Adequacy Statement (NAS)

A statement of nutritional adequacy developed by AAFCO is required on all pet food packages. The nutritional adequacy statement confirms 3 important features of that cat food product:

1. *The product is complete and balanced.* This means that the product is intended to provide all the nutrient requirements as the sole source of nutrition. If the statement reads “intended for intermittent or supplemental feeding” it should not be considered complete and balanced and should be avoided for everyday feeding unless overseen by a veterinarian (as some of the therapeutic diets are labeled). Typical products that are not complete and balanced but may look like a balanced cat food are products with names such as hors d'oeuvres, appetizers, toppers etc. Treats and snacks are other examples and all of these should be used sparingly.
2. *The life stage.* When a product is complete and balanced, the NAS should identify the life stage for which it is intended. AAFCO defines nutrient profiles and feeding trial requirements for growth (including an addition of large breed puppy), reproduction, adult maintenance, and all-life stages only. It is important to remember that there is no AAFCO defined nutrient profile for senior/geriatric life stage and the nutrient content of products marketed for senior pets can vary widely. If a product is formulated to meet AAFCO profiles for “all life stages” it must meet the minimum nutritional requirements for both growth and adult maintenance. Products formulated for “all life stages” may contain excessive amounts of some nutrients, which can result in overfeeding. It is better to feed cats with food designed to match their specific life stage.
3. *Method for determining nutritional adequacy.* Nutritional adequacy can be established by a pet food company either 1) through animal feeding trials or 2) through formulation tests. Feeding trials are conducted with animals to ensure that nutrients in a given food or line of foods are present in sufficient quantities to promote good health *and* are bio-available to the animal ensuring the nutrients are digested properly.
 - a. A product bearing the statement “Product X” **is formulated to meet nutrient profiles established by AAFCO** (species) nutrient profiles for [specified] life stage has had its nutrient content confirmed by mathematical calculations (adding nutrient content of ingredients listed in a database) or by analytic testing of the finished product (preferred). The formulation method does not include testing involving animals.
 - b. A product bearing the statement: “**Animal Feeding tests using AAFCO procedures** substantiate “Product X” provides complete and balanced nutrition for [specified] lifestage, has undergone a feeding trial evaluation. Feeding trials allow for an *in vivo* product evaluation and an indirect measurement of bioavailability of nutrients. Feeding trials are preferable to formulations to help test nutritional adequacy but they do not assure the product provides adequate nutrition under all circumstances.

Caloric Content Disclosure

Because of the prevalence of overweight cats, labeling calories is essential for determining if cat foods meet the energy needs of cats. Fortunately, caloric disclosure is now required on packaging. Cat owners may not be aware of calorie content variation between foods, which can result in obesity and related health problems. Look for companies that report the caloric content in ways easily found on websites and packaging, making it easy to compare products and determine how much to feed a cat. Making calorie content readily accessible greatly helps the veterinary team determine a proper food “dose” (amount to feed) when making a nutritional recommendation.

Ingredients

Evaluation of the ingredient list is often the most controversial aspect when interpreting a pet food label. Buyers are barraged with marketing claims, misinformation and even scare tactics. Unfortunately, the belief that the ingredient list is the most important piece of information when judging cat food quality is reinforced when many of the pet food rating systems and pet food reviews are inappropriately based on judgments about ingredients. With the exception of patients with adverse reactions or primary food allergies, or a traditional Chinese medicine approach, this is often the **least** useful information provided. **Cats require nutrients, not ingredients**, so a food composed of wonderful

sounding ingredients may be less nutritious than one with seemingly less appealing (to the cat owner) ingredients. Unfortunately, the ingredient list is simply not a useful way to evaluate the quality of the cat food. Evaluation of ingredient lists remains challenging because transparency about ingredients, ingredient sources, and processing methods--beyond the minimum of what is legally required--is generally difficult to come by in the cat food industry. In addition, the nutrient-based scientific literature is not comprehensive, especially when compared to the research base for human nutrition.

Although there is widespread misunderstanding about pet food ingredients, the major ingredients commonly used in pet food (beef, poultry by product, lamb meal, etc.) are fairly well regulated and defined by AAFCO. Many fruits, vegetables, and other seemingly healthy ingredients have no AAFCO definition for the ingredient. If an ingredient definition does not exist, AAFCO regulations state that it "shall be identified by the common or usual name." For example, 'Apples' or other fruits may contain seeds, stems, leaves, skins, or pulp. For all of these reasons, reliance on pet food ingredients as the primary way to assess a pet food product would be a poor indicator of a product's overall health impact for a cat. The [Nutrition Reference Manual](#) provides an excellent description of cat food label requirements and clarifications about [ingredient definitions](#).

Nutrition Resources

Another very credible and useful resource about nutrition myths and many other cat nutrition topics is the Tufts Clinical Nutrition blog: [Petfoodology](#). This content is current and written for cat owners. WSAVA has collated a [Nutrition FAQ and Myth](#) fact sheet, and created guides for cat owners to evaluate nutrition information from the internet about [feline](#) nutrition.

Nutrition Recommendation, a Cat-Specific Process

The final steps of making a cat food selection is to use your judgment in evaluating a product and match it closely with the cat's life stage, lifestyle, and overall health. To complete the process, you would continue to monitor the cat's response to make sure you see the expected results--that the cat maintains optimal health and healthy body weight.

Recalls

Sadly, pet food safety issues remain a growing concern. We have become more aware of pet food safety issues, most dramatically evident in 2007 with melamine adulteration of wheat gluten which affected many products and led to renal failure in a number of pets. More recently, products have been recalled for aflatoxin contamination, and several more foods or treats with potential salmonella contamination. Out of these tragedies, have come great changes and improvements.

Pet food safety is now more closely monitored by the FDA, and there are more professional "watch-dogs" sharing information and updates about pet food recalls: Veterinary Information Network (VIN), American Veterinary Medical Association (AVMA), and state veterinary medical associations. There is now a central Food and Drug Administration (FDA) [online safety reporting portal](#) for veterinarians and owners to submit reports of concern about cat foods and treats.

If you have suspicions about the safety of a food, this warrants a thorough review of food eaten by the cat. Check the FDA website and contact the pet food manufacturer to alert and confirm your concerns. You will need information from the product label, so keep the label with the food until the bag is completely consumed.

Commonly Held Beliefs Related to Unique Nutritional Requirements and Feeding Behavior of Cats

Carbohydrates and cats. Cats are obligate carnivores; however, they retain significant metabolic flexibility. The absolute requirements to provide adequate protein and essential fatty acid requirements comprise approximately 50% of the cat's daily calories. Beyond that, cats will need a dietary energy source to provide a source of glucose. In the remaining 50% daily caloric requirement, cat's have great flexibility. Energy can be provided from any of the 3 energy bearing nutrients (carbohydrate, protein and fat). While carbohydrates are not considered essential nutrients for nonreproducing adult cats, carbohydrates can supply an important source of glucose.

Senior Cats

Sarcopenia, age-related lean muscle loss, is common in senior/geriatric cats. Dietary management of feeding an increased protein diet may slow the loss of lean body mass. Elder cats also have an increased caloric requirement compared to young adult and middle aged cats. If there is a decline in weight as these cats age, they may benefit from a higher protein and calorie diet (such as a kitten food). Be aware that there is no established AAFCO nutrient profile for a senior life stage, thus the nutrient composition of products marketed for senior pets varies widely and may or may not be appropriate for a senior cat.

Feeding Behavior

Cats are solitary hunters who hunt and consume small prey. They do not share food (except queens with her kittens). Cats fed inside, especially in a multi-pet household should be treated as solitary feeders providing enough space to prevent competition or stress while eating. Ideally cats would be fed multiple small meals each day, over two meals or free feeding.

Nutrition Resources

World Small Animal Veterinary Association Global Nutrition Committee Tool Kit

<https://wsava.org/wp-content/uploads/2020/01/WSAVA-Global-Nutrition-Toolkit-English.pdf>

Resources for veterinarians (diet history form, caloric requirement charts, etc.)

Resources for pet owners (critical evaluation of information in the internet, selecting a pet food)

American College of Veterinary Nutrition www.acvn.org

FAQ section (How to choose the best diet, how much to feed, natural/human grade terminology, raw foods, safety of foods, supplements, home-prepared diets)

Resources including a diet history form

Directory of diplomates- available for clinical consultation

American Academy of Veterinary Nutrition <https://www.aavnutrition.org>

Provides a list of individuals/institutions that provide nutrition consultation services

Listserv for veterinarians & technicians

Tufts Cummings School of Veterinary Medicine Clinical Nutrition Service

www.petfoodology.org

-Information on pet nutrition, selecting a pet food, ingredients, raw diets, home-prepared diets

-Excellent pet food nutrient calculator http://vetnutrition.tufts.edu/2017/08/nutrient_converter/

Pet Nutrition Alliance <http://www.petnutritionalliance.org/>

Resources include a nutritional calculator for determining calorie needs

Resource includes "Dare to Ask" Manufacturer report, asking select WSAVA criteria

Petdiets.com <http://www.petdiets.com>

Excellent website written by a Board Certified Veterinary Nutritionist® for pet owners (Nutrition Library, FAQs)

Nutrition consultation and diet formulations by Board Certified Veterinary Nutritionists®

Well-referenced article on raw diets: <http://www.petdiets.com/Library/Articles/Dogs/Foods-and-Feeding>

Weeth Nutrition <http://weethnutrition.wordpress.com>

-Excellent website written by a Board Certified Veterinary Nutritionist® for pet owners

The Ohio State University Veterinary Medical Center <http://vet.osu.edu/vmc/nutrition-support-service>

Includes a basic calorie calculator, how to choose a diet, understanding pet food labels, myths

FDA Pet Food Site <http://www.fda.gov/AnimalVeterinary/Products/AnimalFoodFeeds/PetFood/default.htm>

Information on FDA regulation of pet food with links to food safety, recalls, pet food labels, selecting foods

FDA link for recall information:

<http://www.fda.gov/AnimalVeterinary/SafetyHealth/RecallsWithdrawals/default.htm>

Review this FDA link for information on raw pet foods:

<https://www.fda.gov/animal-veterinary/animal-health-literacy/get-facts-raw-pet-food-diets-can-be-dangerous-you-and-your-pet>

The American Veterinary Medical Association

Recalls & Alerts: https://www.avma.org/search?search=recall&sort_by=created&f%5B0%5D=content_type%3Arecall

Review article on raw meat-based diets (12/13): <https://avmajournals.avma.org/doi/pdf/10.2460/javma.243.11.1549>

CDC (Centers for Disease Control and Prevention) Site

<https://www.cdc.gov/features/pet-food-safety/index.html>

Information on proper handling of pet foods, information on feeding raw foods

AAFCO (Association of American Feed Control Officials) Talks Pet Food

<http://talkspetfood.aaafco.org>

Discusses how to read a pet food label, selecting a pet food, ingredients, safety, regulation of pet food, etc.)

Foodsafety.gov <http://www.foodsafety.gov/keep/types/petfood/>

Federal Food Safety information site has a section on pet foods that links to additional information regarding tips for buying, preparing, and storing pet food.

Consumer Lab <https://www.consumerlab.com>

Independent testing of human and some veterinary supplements

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Complicated Endocrine Cases
Cynthia Ward, VMD, PhD, DACVIM (SAIM)

Concurrent Hyperthyroidism and Chronic Kidney Disease

Overview of the Issue

Hyperthyroidism is a common and insidious endocrine disease affecting middle to older-aged cats. Although some cats may present with a combination of the classic clinical signs of weight loss despite a good appetite, vomiting, polyuria/polydipsia, hyperactivity, and diarrhea, it is common to see relatively asymptomatic cats that have been identified as hyperthyroid. This is because of an increased awareness of the disease by veterinarians and also because of the inclusion of Total T4 (T4) measurements on geriatric blood screen panels. Greater than 90% of cats are diagnosed with hyperthyroidism based on an elevated serum T4. An elevated serum T4 approaches 100% sensitivity so if it is found, the cat can be presumed to be hyperthyroid if there has been no laboratory error. Hyperthyroid cats often have concurrent diseases one of which is chronic kidney disease (CKD). There is no causal relationship between hyperthyroidism and CKD that has been documented; however, as they are both common in older cats, it is not surprising that they are often found in the same animals.

Key Clinical Diagnostic Points

Once the diagnosis of feline hyperthyroidism is made, the cat should be treated even if relatively asymptomatic. Untreated hyperthyroidism can lead to heart and multi organ failure; therefore, treatment should not be delayed. It has been well established that thyroid hormone supports renal GFR and that treatment of hyperthyroidism can unmask CKD that has previously been undiagnosed. Therefore, kidney function must be thoroughly evaluated before hyperthyroidism treatment is planned. Before treatment is initiated for feline hyperthyroidism, a minimum database including a CBC, Chemistry profile, and urinalysis should be performed. These data will identify concurrent diseases that must be addressed and allow for further renal function evaluation. Chest radiographs, cardiac ultrasound, or abdominal imaging should be performed in cats that may have suspected respiratory, heart, gastrointestinal, or renal disease. For cats with CKD, treatment protocols may be modified so that thyroid levels do not decrease too precipitously in order to preserve renal function. However, the presence of CKD should not prevent treatment of hyperthyroidism.

Key Therapeutic Points

Treatment for feline hyperthyroidism should be initiated when the disease is identified as recommended above. Radioactive iodine (^{131}I) is the treatment of choice for hyperthyroid cats. It is safe, effective, and has virtually no side effects. It requires an expense up front which usually evens out cost-wise over medical therapy after 1.5-2 years. The convenience and assurance that the animal will not have thyroid hormone spikes if medication is missed make this treatment highly attractive. The cat-owner bond may be maintained without constant struggle in cats that are tough to medicate. Cats must be quarantined after receiving ^{131}I . The time period varies according to state or institutional regulation. Ninety-five percent of cats treated with ^{131}I will be controlled after 1 injection, although as cats have been living longer after ^{131}I treatment they may need a second treatment years later. Scintigraphy prior to ^{131}I is recommended so that the dose can be tailored to the individual cat; lower doses of ^{131}I are recommended to prevent hypothyroidism. Optimally, serum T4 levels should not decrease below 1 mcg/dl and TSH levels should remain normal after treatment in order to preserve renal function. If this happens, treatment with levothyroxine (0.05 mg sid) may be instituted until serum T4 levels stabilize. This usually occurs after 2-4 months. The rare cat becomes permanently hypothyroid post- ^{131}I injection may require lifelong levothyroxine supplementation.

Methimazole is a thioureylene compound effective in controlling elevated serum T4 levels and clinical signs associated with hyperthyroidism. It prevents iodine incorporation into tyrosyl groups on the thyroglobulin molecule; thereby, preventing the synthesis of active hormone. It is a relatively inexpensive compound that allows owners to see the benefits of treating hyperthyroidism without committing to the expense and hospitalization required by ^{131}I therapy. It is effective in controlling elevated serum T4 levels and the clinical signs associated with hyperthyroidism. Methimazole is available in pill, liquid, and transdermal ointment formulations. There is a FDA veterinary approved compound, FelimazoleTM, that is available in coated 2.5 and 5 mg tablets. If using the human product (TapazoleTM), owners should be warned to wear gloves and wash their hands thoroughly if the pills are broken. Methimazole should be administered twice a day for optimal control. It is a highly antigenic compound and side effects can be serious. Mild side effects include transient anorexia, vomiting, and anorexia. These usually subside within the first 1-2 weeks of therapy. More serious side effects include facial excoriations, hepatic toxicity, leukopenia, thrombocytopenia, positive ANA. If any of the more serious side effects occur, methimazole should be discontinued. Methimazole therapy also has the benefit of being able to titrate the medication so that renal function can be

preserved. For instance, if the hyperthyroid cat is already in renal failure, methimazole should be started at half the normal starting dose. Serum T4, BUN, and Creatinine levels can be checked after 7 days of treatment to determine how well the methimazole dose is controlling the hyperthyroidism and what effect the lowering of the GFR had on renal function.

The Y/D™ is severely limited in iodine content. Since iodine enters the body through the GI tract, Y/D™ controls serum thyroid levels by not allowing the body's iodine levels to support excess active thyroid hormone production. Care must be taken to ensure that the hyperthyroid cats eat only the Y/D™ diet. If they have access to even minute amounts of normal cat food or other iodine-containing organic matter (such as rodents or bugs), thyroid hormone levels can rise quickly. This rapid rise in active thyroid hormone may precipitate a thyroid storm. Y/D™ is perfectly suited for a mildly affected indoor-only cat that cannot be given daily medication. Y/D is meant to be a sole therapy and should not be used in conjunction with methimazole or ¹³¹I therapy.

Beta-adrenergic receptor blockers, such as atenolol, may be used to prevent cellular toxic effects of excess thyroid hormone in cats with concurrent renal failure. In these cats, anti-thyroid medications may be used at decreased doses in order to preserve some T4-supported GFR. In these cases atenolol at 0.625 mg sid will block the thyroid hormone attenuation of catecholamines on the cells. Atenolol will prevent thyroid storm in hyperthyroid cats that may occur with acute withdrawal of anti-thyroid medication or as a result of thyroid gland manipulation. Amlodipine can be used to manage hypertension that is refractory to anti-thyroid treatment.

Monitoring

The treatment goal in the cat with hyperthyroidism and CKD is to keep thyroid hormone in a normal range while not worsening CKD. T4 should be maintained in the mid normal range. If TSH can be measured, then it should be in the normal range as well. TSH is a better way to monitor thyroid function; however, the veterinarian is limited by the availability of a sensitive assay for TSH in cats.

Key Drug	Drug Class	Dose Range	Frequency	Route	Indications
Methimazole Felimazole ^R	Thiourelene	1.25-2.5 mg/cat	bid	PO Transder	Lower dose is indicated in CKD
Atenolol	Beta-blocker	6.25 mg/cat	Q 24h	PO	¹³¹ I therapy d/c methimazole
Amlodipine	Ca channel blocker	0.625-1.25 mg/cat	Q 24h	PO	Hypertension
Telmisartan	Angiotensin receptor blocker (ARB)	2 mg/kg	Q24h	PO	Hypertension

Summary including 5 KEY “TAKE HOME” POINTS

- 1. Always treat hyperthyroidism in cats as untreated disease can be fatal
- 2. Begin methimazole therapy at the low end of the dose when treating hyperthyroid cats with CKD
- 3. Monitor and treat hypertension that does not resolve with hyperthyroid treatment

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Secrets to Managing Today's Diabetic
Cynthia Ward, VMD, PhD, DACVIM (SAIM)

Diabetes mellitus is a common endocrinopathy in cats. Cats usually get type 2 or the non-insulin dependent form of the disease. This occurs as a result of insulin-resistance, for which major risk factors are obesity, increasing age, male gender, physical inactivity, and glucocorticoid use. The pancreatic beta cells are forced to produce increasing amounts of insulin to overcome the resistance, resulting in ultimate loss of function in the cells. Additional loss results from direct glucose toxicity of the beta cells. As part of the insulin resistance spectrum, cats may go into diabetic remission, meaning that they remain euglycemic without use of insulin. This is probably due to resolution of the factors resulting in insulin resistance. Many of these cats will return to insulin dependence later in their lifetimes. Aggressive insulin therapy with an appropriate long-acting insulin along with treatment of concurrent disease results in the greatest chance of achieving remission.

Diagnosis

Diabetes mellitus is relatively easy to diagnose. Clinical signs include polyuria/polydipsia, weight loss, persistent or recurrent urinary tract infections, weakness and muscle wasting, and peripheral neuropathies. Diagnosis can be made by recognition of appropriate clinical signs, and demonstration of persistent hyperglycemia and glucosuria. One confounding factor to this diagnosis is stress. Stress, alone, can cause hyperglycemia, that can be high enough to be cause spill over into the urine and glucosuria. Should the clinician have any doubt of whether hyperglycemia and glucosuria are due to diabetes mellitus, s/he should check a serum fructosamine level. This value gives the average of the blood glucose over the preceding 2-3 weeks. If elevated, then diabetes mellitus can be diagnosed. If not elevated, then the hyperglycemia/glucosuria was probably due to stress.

Initial evaluation will decide how intensively the patient should be managed as diabetic treatment is begun. If the animal is eating and drinking normally and is well hydrated, there is no reason to hospitalize him/her while insulin therapy is initiated. If the animal is ketotic, acidotic, hyperosmolar, or dehydrated, s/he should be admitted to the hospital and stabilized before long term insulin therapy is instituted. Concurrent diseases seen with diabetes mellitus include: urinary tract infections, endocrinopathies such as acromegaly, hyperadrenocorticism, and hyperthyroidism, pancreatitis, and pregnancy.

Initial evaluation of the diabetic animal should include a complete physical examination, CBC, chemistry profile, urinalysis, and T4. A urine culture should be considered even if urinalysis and sediment parameters are normal since up to 35% of urinary tract infections can be clinically silent in animals with dilute urine. Abdominal imaging may be pursued if clinically indicated. Concurrent medical conditions should be addressed aggressively so that the diabetes mellitus can be more easily controlled.

Treatment

Diabetes mellitus can be frustrating, expensive, and time-consuming for owners to treat. Because our patients do not live as long as humans, veterinarians do not have to worry about keeping blood glucoses within the tight range required for human diabetes management. Our goals of therapy, therefore, can be less rigorous, thereby alleviating some of the burden to our clients. Our goals of therapy should be correction of clinical signs, control of concurrent diseases, and avoidance of emergency situations such as hypoglycemia, ketosis, and hyperosmolality. It is beneficial to have an in-depth discussion with the owner as to the time and effort s/he can realistically commit for diabetic control for the pet. It is important to establish a good rapport with diabetic owners since they will be asked to provide invasive (injections) and time-consuming (glucose monitoring) care for their pets. We want owners to be honest about what they can and can't do. Often the veterinary nurse can make owners feel more comfortable and more willing to admit problems they will have with diabetic care.

Stable cats with blood glucoses less than 400 mg/dl may be treated initially with a diet change. Cats are very carbohydrate intolerant, and a low carbohydrate diet can result in euglycemia in some cats. Prescription diets are recommended; however, if the owners can't or won't commit to these diets, commercial diets can be used. Canned diets tend to be lower in carbohydrates and some websites include carbohydrate data on specific diets. Practitioners should be aware that ingredients in over-the-counter cat foods can change, so carbohydrate data needs to be updated regularly. Because of the deleterious effects of a hyperglycemic environment on the cat pancreas, diet change alone should not be tried for more than 2 weeks. If the cat has not become euglycemic over that time period, then insulin therapy should be instituted. Insulins recommended for cats include: ProZinc[®] glargine (Lantus[®]), and Vetsulin[®]. ProZinc[®] and Vetsulin[®] insulins are labeled for veterinary use. Tujeo[®], a long acting U-300 glargine insulin, may provide longer duration of action that may be helpful in some hard-to-control cats. NPH insulin may be

used but it does not have the duration of action in cats to allow bid treatment. Optimally NPH needs to be given tid-qid in cats. The starting dose of insulin (regardless of type) in cats is: 0.25-5 U/kg bid. Some insulins such as ProZinc^R or Tujeo^R may be suitable for sid treatment. In this case the starting dose should be at the higher end of the dosing range.

Meal-fed cats should be fed twice a day when insulin is given. Their calories should be strictly controlled. If the cat does not eat normally, half the dose of insulin should be given. Many owners give insulin while the animal is eating. This makes the insulin injection a pleasant experience for the pets and easier for owners to treat the animal. Some cats prefer to nibble food throughout the day. These grazers can often be well managed by allowing them free choice eating with insulin injections twice per day. Care should be taken to ensure that the cats are not receiving more than their caloric needs since extra weight should be avoided.

Exercise is beneficial to diabetics and serves to lower insulin requirements and provide better glycemic control. Walking outdoors, cat play, or hiding food in the house can be effective ancillary treatments for diabetes mellitus. Average time for initial diabetic control is 6-8 weeks.

Monitoring

Veterinarians should remind owners of the goals of diabetes treatment: control of clinical signs, maintaining good energy levels and muscle conditioning, and avoidance of emergencies. It is not necessary to keep blood glucose levels in a tight range as long as the animal is doing clinically well. After insulin is started, the veterinarian should wait 7-14 days to monitor any effects since it takes this long for the animal to adjust to insulin therapy. During that time period owners may measure urine glucose and ketones. They do not need to collect urine, but may put the ketodiastix into wet areas in the litter box. They should call if there are more than 3 negative urine glucose readings or if the ketones are positive. If urine glucose is negative, one doesn't know if the blood glucose is 40 or 290 mg/dl; the renal threshold for glucose in the cat is approximately 300 mg/dL. Alternatively, the owner can use a portable glucometer and measure blood glucose directly. Insulin doses should not be changes as a result of readings, but owners should call if the animal is ketotic or hypoglycemic.

At the initial recheck, the veterinarian should question the owner about resolution of clinical signs. A physical exam and weight measurement should be completed. In this way the veterinarian can evaluate the clinical response to insulin.

Serum fructosamine levels have been advocated for use in monitoring insulin response. Fructosamine is a molecule formed by a steady-state reaction between serum albumin and glucose and it represents the average blood glucose over the preceding 2-3 weeks. For fructosamine to be interpretable, the pet should have been on a stable insulin dose for at least 3 weeks before the fructosamine is taken. Fructosamine levels can be useful; however, it is inappropriate to use in unstable animals or those in which a somogyi, also termed hypoglycemic-induced hyperglycemic, response is suspected. For these patients, a glucose curve must be completed.

Glucose Curves

A glucose curve is the only way to truly evaluate the body's response to insulin. Important information obtained from glucose curves includes the onset of action of the insulin, the duration of action of the insulin, the time of peak activity of the insulin, and how low the glucose goes (nadir). The first three parameters indicate whether the right type of insulin is being used; the last parameter gives information about the dose of insulin used.

This technique involves hospitalizing patients to have blood glucose measurements typically every 2 hours, but up to every 1 hour if necessary. This traditional glucose curve has many limitations, including disruption of the patient's normal activity and eating routine, the introduction of stress-related hyperglycemia, and labor intensiveness of the procedure. The use of long-acting insulins such as ProZinc^R Glargine^R, Determir^R, and Tujeo^R may also necessitate a 24-hour glucose curve to fully evaluate their efficacy in some animals. Furthermore, diabetic cats have been shown to have significant variations in their day-to-day glycemic control. Intermittent blood sampling over only a 12-hour period may grossly over or underestimate a patient's glycemic control, and glucose peaks and nadirs may be missed if they occur between samplings.

Continuous interstitial glucose monitoring systems (CGMS) have been approved by the United States Food and Drug Administration for use in human diabetics and measure interstitial glucose using an electrochemical reaction that is then correlated to serum glucose concentrations by algorithm. Interstitial glucose has been shown to correlate well with plasma glucose levels, and the relationship between plasma glucose and interstitial glucose is not affected by insulin. These systems are comprised of an external sensor with a flexible electrode that reacts with glucose when it is inserted into the subcutaneous tissue. There are two systems that have been validated for use in veterinary patients: the MiniMed iPro^R and the Abbott FreeStyle Libre^R. The FreeStyle is disposable, cheaper, and more

convenient to use and is a flash system in which the glucose data is stored in a sensor and then transferred to a reader upon passing over the sensor. It also does not require at home blood glucose calibrations. The FreeStyle Libre can be applied to cats who then go home; glucose curve data is collected in the pets' home environment. The Libre last approximately 2 weeks and may be replaced at any time after they stop collecting data. The data is uploaded onto a database and can be shared with the veterinarian. In both systems glucose data is averaged and reported every 5 minutes.

Although the FreeStyle Libre systems can be useful for evaluation of insulin therapy in many pets, they are not appropriate for everyone. Some owners are prompted to make insulin adjustments based on a single day's data; data can vary from day to day and the most helpful information is the averaged glucose measurements over an entire week.

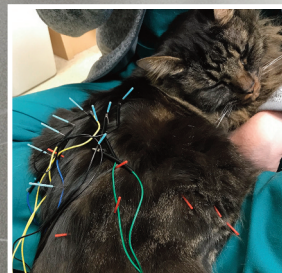
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