AMERICAN ASSOCIATION OF FELINE PRACTITIONERS

2022 Spring into Feline Medicine

Sunday, April 24th | Wednesday, May 4th | Saturday, May 14th

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

American Association of FELINE PRACTITIONERS®

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Purrfecting Strategy & CommuniCATion in the FURst Kitten Visit
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Spring Into Feline Medicine

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AAFP Headquarters

American Association of Feline Practitioners
750 Route 202, Suite 200
Bridgewater, NJ 08807
Phone: (800) 874-0498
Email: info@catvets.com
Web: www.catvets.com
Web: www.catfriendly.com

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THREE-DAY **VIRTUAL LIVE CE EVENT**

Sunday, April 24th | Wednesday, May 4th | Saturday, May 14th

ALL TIMES ARE EASTERN TIME ZONE

Sunday, April 24, 2022

TIME	SESSION TITLE	SPEAKER	SPONSOR
12:00 - 1:00 pm	Diagnostic & Therapeutic Approach to Feline URI	Dr. Mike Lappin	Boehringer Ingelheim
1:20 - 2:40 pm	Purrfecting Strategy & CommuniCATion in the FURst Kitten Visit	Dr. Natalie Marks	zoetis
3:00 - 4:20 pm	Feline Fracas: Why Cats Fight & How to Help Them	Dr. Theresa DePorter	
4:30 - 5:30 pm	Easy as One, Two, Pee: Steps for Solving Feline House-Soiling	Dr. Julia Albright	Purina Pro Plan Veterinary Diets

Wednesday, May 4, 2022

TIME	SESSION TITLE	SPEAKER	SPONSOR
2:00 - 3:00 pm	Diagnosis & Treatment of Proteinuria in Cats	Dr. Stacie Summers	Royal Canin
3:15 - 4:15 pm	Ionized Calcium in Cats: How Much are You Missing Without This Measurement?	Dr. Dennis Chew	zoetis
4:45 - 5:45 pm	Should You Extract This Tooth? Using Diagnostics to Decide (Probing, Intraoral Radiography, & CBCT)	Dr. Jan Bellows	Dechra
6:00 - 7:00 pm	Role of Dietary Phosphorus in Feline Renal Health & in Management of CKD	Dr. Stacie Summers	Royal Canin

Saturday, May 14, 2022

TIME	SESSION TITLE	SPEAKER	SPONSOR
12:00 - 1:20 pm	Hospice & Palliative Care: The Foundations for the Role of the GP	Dr. Mary Gardner	Lap of Love
1:40 - 2:40 pm	The Old Cat in the Clinic: How Senior Wellness Visits Improved Charlie's Quality of Life	Dr. Myles McKenna	zoetis
2:50 - 3:50 pm	The Itchy Cat	Dr. Mike Rossi	Ceva
4:00 - 5:00 pm	Frustrating Felines: Inappetant Cats	Dr. Diane Delmain	Purina Pro Plan Veterinary Diets

American Association of Feline Practitioners
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Diagnostic & Therapeutic Approach to Feline URI

Michael R. Lappin, DVM, PhD, DACVIM

Abstract. There are many causes of bacterial, viral, and fungal causes of upper respiratory infections (URI) in cats. The primary purpose of this presentation is to update attendees on management of cats with chronic disease that is likely induced by bacterial or viral causes.

Key points

1. The most common primary bacterial infections are due to Bordetella bronchiseptica, *Mycoplasma* spp., and *Chlamydia felis*.
2. The most common viral infections are feline herpesvirus 1 and feline calicivirus.
3. Amoxicillin or doxycycline are the best antibiotics to try for acute bacterial infections.
4. It can be difficult to interpret results of PCR assays on discharges in cats with upper respiratory infectious because of vaccines and subclinical carriers.
5. Lessening stress can lessen recurrent upper respiratory tract infections in cats.

Essential points in client education. In acute upper respiratory infections in cats, treatment may not be needed. If signs of infection last more than 10 days, a complete diagnostic workup should be completed. Making the home less stressful can lessen recurrent signs of upper respiratory disease.

Key words. Feline, herpesvirus, calicivirus, PCR, famciclovir

Please see the ISCAID respiratory treatment guidelines for further information on this very important topic.

Lappin MR, Blondeau J, Boothe D, Breitschwerdt EB, Guardabassi L, Lloyd DH, Papich MG, Rankin SC, Sykes JE, Turnidge J, Weese JS. Antimicrobial use Guidelines for Treatment of Respiratory Tract Disease in Dogs and Cats: Antimicrobial Guidelines Working Group of the International Society for Companion Animal Infectious Diseases. J Vet Intern Med. 2017;31:279-294.

Bacterial causes. Almost all cats with chronic mucopurulent or purulent nasal discharge have a bacterial component to their disease. Diagnosis and treatment was reviewed by the International Society for Companion Animal Infectious Diseases.[1] Primary bacterial disease is rare but may be associated with *Bordetella bronchiseptica*, *Mycoplasma* spp., *Chlamydia felis*, and some *Pasteurella* spp..[1] Recently it was shown that *Bartonella* spp. are not a causes of chronic rhinitis in cats.[2]

Most cases of chronic or recurrent bacterial rhinitis are secondary to other diseases including trauma, neoplasia, inflammation induced by viral infection, foreign bodies, inflammatory polyps, and tooth root abscess. Thus, if routine antibiotic therapy fails with doxycycline or amoxicillin, a diagnostic workup should be performed.[1] If the diagnostic workup fails to find a primary disease and neutrophilic or mixed inflammation is noted, other antibiotics could be considered.[1] Pradofloxacin has been evaluated as a treatment of feline rhinitis and conjunctivitis in several studies and can be considered as a rescue drug for cats with suspected bacterial disease.[3,4] This fluoroquinolone is known to be safe for the use in cats.[5]

In a placebo-controlled, double-blind clinical trial, 39 cats with signs of bacterial upper respiratory infections or conjunctivitis were entered.[4] The cats were randomly entered into 1 of 2 treatment groups: treated orally with either 5 mg/kg pradofloxacin q24hr or 5 mg/kg doxycycline q12hr for 42 consecutive days.[4] Changes in health status and clinical scores were evaluated. The presence of *C. felis* and *Mycoplasma* spp. DNA was determined by quantitative polymerase chain reaction (PCR) and nested PCR of conjunctival swabs, respectively. Prior to treatment, DNA of *C. felis* and *Mycoplasma* spp. was amplified from samples from 23 and 20 cats, respectively. Clinical signs improved markedly within the first week for cats of both groups. Complete elimination of *Mycoplasma* spp. DNA was achieved in both groups. During treatment with either drug, *C. felis* DNA copy number declined quickly, all cats administered doxycycline became *C. felis* DNA negative and 4 cats treated with pradofloxacin remained *C. felis* DNA positive. In this study, it was concluded that both pradofloxacin and doxycycline have good efficacy against *C. felis* and *Mycoplasma* spp., resulting in a marked improvement of clinical signs. The study showed evidence that the pradofloxacin protocol studied may eliminate *Mycoplasma* spp. infections. However, since *C. felis* DNA was still amplified from samples from some cats after treatment with pradofloxacin, infection might not always be eliminated using this protocol.

Since bacterial rhinitis leads to chondritis and osteomyelitis, antibiotic therapy may need to be continued for weeks in cats with chronic disease. Drugs with an anaerobic spectrum that also penetrate bone and cartilage well are often effective. Clindamycin or amoxicillin-clavulanate are frequently used. Amoxicillin-clavulanate has the advantage of killing most *B. bronchiseptica* isolates. Clindamycin has the advantage of effective against *Mycoplasma* spp. and is effective against many anaerobes. After being administered twice daily on the first day, azithromycin can be administered every third day.[1] Cefovecin can be used in cats that are difficult to treat orally, but since it is a beta-lactam, there is no effect against *Mycoplasma* spp..[6] Topical administration of antibiotics by drops or nebulization may be beneficial for some cats but controlled studies are generally lacking. Lessening stress and immune stimulants as discussed for viral disease may be of benefit.

Viral diseases. Herpesvirus 1 (rhinotracheitis; FHV-1) and calicivirus (FCV) are the most common viral causes of sneezing and nasal discharge in the cat. If oral ulcers are present, calicivirus is most likely. If corneal ulcers are present, herpesvirus 1 is most likely. FHV-1 has now also been associated with chronic stomatitis, facial dermatitis, and endogenous uveitis. Viral rhinitis with or without secondary bacterial infection can be recurrent. FHV-1 can be documented by direct fluorescent staining of conjunctival scrapings, virus isolation, or polymerase chain reaction. Since FHV-1 DNA can be amplified in conjunctival cells of approximately 25% of healthy cats, the positive predictive value of these tests in diseased cats is low.[7] Quantitative PCR may ultimately prove to correlate to the presence or absence of disease but some cats with chronic FHV-1 infections do not have high values.[8,9] Currently used PCR assays also detect vaccine strains of FHV-1. RT-PCR assays can be used to amplify the RNA of FCV. However, these assays have the same problems with predictive value as those to detect DNA of FHV-1.

Feline viral rhinitis with or without secondary bacterial infection can be recurrent. There are no consistently effective primary therapies. For FHV-1, lysine at 250-500 mg, PO, once or twice may be helpful in some cats lessening recurrent disease and has been shown to be safe but should be given as a dose, not fed with food and is not a treatment for active disease. Lysine has been shown to be ineffective for prevention of upper respiratory tract infections in shelter studies and so should not be used for this purpose.[10]

Administration of human alpha 2b interferon at 50 U, PO, daily may help some cats with suspected chronic calicivirus or FHV-1 infection. This can now be formulated for practitioners by prescription at some pharmacies (www.roadrunnerpharmacy.com/) in the USA. In Europe, feline interferon may be beneficial in the management of some cats. Intranasal administration of modified live, intranasal FHV-1 and FCV vaccines may lessen disease in some chronically infected cats.[11] If there is a positive response to intranasal vaccination in a cat with chronic disease, I will use this form of immunotherapy up to 3 times per year.

Famciclovir is currently the orally administered drug of choice for management of acute (and possibly chronic) FHV-1 infections in cats.[12-14] The drug has been prescribed mostly at 40 or 90 mg/kg and is safe at up to 90 mg/kg, PO, q8hrs and so the dose should be increased if lower doses were used and the initial response is suboptimal and FHV-1 is still suspected. Administration of one dose of famciclovir (125 or 500 mg) on admission to an animal shelter was ineffective in lessening clinical signs of disease.[15]

Topical cidofovir (product for humans) can be used for the treatment of FHV-1 conjunctivitis twice daily and was effective in a controlled research project.[16] The drug is easier to administer (twice daily) than idoxuridine or other anti-FHV-1 ocular therapies and does not cause as much irritation. This drug is available in some compounding pharmacies (www.rxfixer.com). In a recent research study, raltegravir was effective for the management of FHV-1 associated clinical signs in a model.[17]

Immune modulation with the probiotic *Enterococcus faecium* strain SF68 (FortiFlora®, Purina Pet Care) was effective in lessening stress reactivated FHV-1 signs in a model.[18] Field studies with this probiotic are in progress. Recently, the use of an intranasal product containing 2 Toll-like receptor agonists was beneficial in lessening signs and shedding of FHV-1 in a model.[19] Field studies with this compound are in progress.

Stress relief. Many of the cats with chronic recurrent signs of upper respiratory disease are likely to be infected by FHV-1 or FCV. Stress reactivation of feline viral infections is thought to be common, in particular for FHV-1. All the principles of stress relief for management of feline interstitial cystitis also apply to cats with recurrent signs of URI. In a recent study, use of a facial pheromone diffusor could lessen recurrent signs of FHV-1 in a mild stress model in experimentally inoculated cats.[20]

Fungal diseases. *Cryptococcus neoformans*, *C. gattii*, and *Aspergillus* spp. are the most common causes of fungal infection in cats. Aspergillosis in cats carries a grave prognosis.

Cryptococcosis is the most common systemic fungal infection of cats and should be considered a differential diagnosis for cats with respiratory tract disease, subcutaneous nodules, lymphadenopathy, intraocular inflammation, fever, and CNS disease. Infected cats range from 6 months to 16 years of age, and male cats are over represented in most studies. Infection of the nasal cavity is reported most frequently (56.3 to 83.0% of cases) and commonly results in sneezing and nasal discharge. The nasal discharge can be unilateral or bilateral, ranges from serous to mucopurulent, and often contains blood. Granulomatous lesions extruding from the external nares, facial deformity over the bridge of the nose, and ulcerative lesions on the nasal planum are common. Submandibular lymphadenopathy is detected in most cats with rhinitis. Definitive diagnosis of cryptococcosis is based on antigen testing or cytologic, histopathologic, or culture demonstration of the organism. Cats with cryptococcosis have been treated with amphotericin B, ketoconazole, itraconazole, fluconazole, and 5-flucytosine alone and in varying combinations. Good to excellent treatment responses in cats were seen with fluconazole (96.6%), itraconazole (57.1%), and ketoconazole (34.6%). Because of toxicity, I no longer use ketoconazole. I generally use fluconazole at 50 mg/cat per day because it has the least side-effects and or the azoles, has the best penetration across the blood-brain and blood-ocular barriers. If life-threatening infection is occurring or the cat is failing to respond to the azole, drugs liposomal amphotericin B should be used. Care should be taken if voriconazole is used as it has been associated with neurotoxicity in cats. Nasal and cutaneous cryptococcosis generally resolve with treatment; CNS and ocular disease are less likely to respond to treatment. Treatment should be continued for at least 1 to 2 months past resolution of clinical disease. People and animals can have the same environmental exposure to *Cryptococcus spp.* but zoonotic transfer from contact with infected animals is unlikely.

Parasitic diseases. While nasal mites (*Pneumonyssoides*) and a nasal worm (*Eucoleus*) occur in dogs in the United States, there are no significant nasal parasites in cats of the USA.

NOTES:

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PURRfecting Strategy & CommuniCATion in the FURst Kitten Visit

Natalie L. Marks, DVM, CVJ

I want to thank Zoetis for their sponsorship of my lecture and for their ongoing commitment to excellence in research and continued education

For millions of pet parents, this is what the pandemic looked like – laying on the couch, watching Netflix and snuggling with a brand-new adorable kitten! Who wouldn't want this? I wish I could be passing around kittens right now for everyone – it's an instant warm fuzzy, a blood pressure reducer, and life's just better when we pet our pets. However, we fall into this snuggle trap in the exam room too and miss a tremendous opportunity to shape the life of that kitten and the many first-time pet parents that are holding the carrier. We just aren't seeing enough cats at veterinary hospitals, and this needs to change.

For most of us, it's a bigger problem than we thought. According to data from VetStreet, less than 2 out of 5 cats see a veterinarian (as compared to 4 out of 5 dogs) [1]. And even less of those are on any kind of preventive care program. And, in the time we do spend with kittens especially, we don't do a great job of teaching normal cat behavior and what abnormal looks like to a pet parent. This education gap often allows kittens to become cats with behavior problems, and behavioral problems create an increased risk for relinquishment to shelters.

There's a rapid domino effect from first not knowing what normal cat behavior looks like, to the behavioral problems that ensue, and then the final fallout displays as a weakened human-animal bond[2]. A foundational study in JAVMA looked at risk factors for relinquishment of cats to shelters, and one of the more common reasons was a pet parent reporting their cat didn't give enough 'physical affection.' What are your thoughts on this? Is that true or is that the perception of a pet parent who can't appreciate and understand feline body language when a kitten or cat says, "I need my space, mom?" Either way, the bond diminishes, pet parents become less engaged, and they are more likely to miss subtle signs of disease.

So, what's the secret sauce? How do we change all of this? Drum roll…. it's the kitten visit! We know that kittens are TWICE as likely to come in for a veterinary exam as compared to any other age group each year. And we know that many pet parents start the kitten journey excited and ready to learn and establish good habits. This is really the ideal time to set up the kitten-to-adult-to-senior cat healthcare journey and increase compliance.

We are a profession of list makers, aren't we? Well, at least I am! Here are my top ten ways to "catapult that kitten visit" into 30 minutes of awesomeness. Yes, I said 30 minutes, and that's necessary for making this work. We can't do what we need to do in 10, 15 or even 20 minutes. Carve out this time now and it will MORE than pay for itself in the future.

Here are the ten ways we'll discuss:

1. Food Textures – All Are Welcome
2. Parasites and 'Indoor Only' Cats
3. Scratching Post Training
4. The Vaccine Experience
5. The Purrfect Pedicure
6. Throw Away the Food Bowl
7. Cat Carrier Coffee Table
8. Enrichment from Day ONE
9. Send Them to School!
10. Preparing for the Future

But before we delve into each specific topic, remember this VERY important piece for your times with these families. Whether it's in the exam room, on the phone curbside, over email, or even video chat, our clients WANT clarity and specific guidance. In fact, according to a JAVMA study looking closely at how clients responded to veterinarians and their treatment plans, pet owners were found to be SEVEN times more likely to comply following a clear recommendation[3].

Food Textures – All Are Welcome

For me, my mind always goes to food first, and nutrition is always one of the top questions and web searches for most pet parents, so let's start here. Two big mistakes many of us make as veterinarians are being too vague when

recommending a food OR strictly recommending only ONE texture of food to kittens. It will help greatly to have pet parents and veterinarians both on the same page here – ALL food textures are welcome and encouraged!

Jennifer Larsen, an assistant professor of clinical nutrition at the Veterinary Medical Teaching Hospital at the University of California, Davis, guides us on some key points about kitten nutrition. “Kittens can have up to triple the energy needs of adult cats which means they want to eat at least 3-4 meals a day with a higher requirement for protein, minerals, and some vitamins. Giving a variety of foods and textures helps small kittens with even smaller teeth eat more efficiently and soften the dry food for easier chewing. And bonus for us, it may help ease the transition to a prescriptive diet later in life!”

We also need to make sure to include in a kitten pack and on our resource pages (and social platform too when possible!) the toxic foods to avoid with kittens, like grapes/raisins, coffee and tea, garlic, onion, and chocolate.

Parasites and ‘Indoor Only’ Cats
Staying in the same vein of prevention, let’s talk about one of the harder conversation pieces with cat parents - the “indoor only” kitten or cat and where on earth would they be exposed to parasites?

This statistic is startling, sad, and humbling for all of us. Knowing what we know about parasitism and even with the obligation to be public health stewards and educators about zoonotic diseases, only 1 in 5 (22%) of cats that visit the veterinarian (representing only 7% of cats in the US) receive parasite protection from that veterinarian. Let’s do better, we CAN do better as a profession.

Want more truth? One in four cats infected with heartworms are described as ‘indoor only’[4]. Mosquitoes aren’t polite – they let themselves inside any chance they get!

As a parent of three human kids, one of which is immunosuppressed, this statistic scares me the most! According to the 2021 data out of CAPC, one in twenty cats are positive for roundworms in the US[5]. While this isn’t kitten specific, it’s what happens when we don’t guide and help form consistent parasite protection habits in our kitten patients and families. Even if the plan is for these kittens to stay indoors, we know cats see the outside world many ways, including:

- Living with housemates who go outdoors
- Killing and eating bugs that serve as transport or hosts for parasites
- Contaminants and feces traveling inside on shoes

These facts are why we need to change the history component of our exams to an ‘exposure conversation.’ While we have almost unanimously asked pet parents if their kitten was ‘indoor or outdoor,’ let’s change the questions to ask about exposures.

- Do they walk their kitten on a harness outside?
- Use cat backpacks?
- Keep their windows open?
- Live with other housemates?
- Or have they created a catio in their home (in which I think I would be happy living in too!)

Enough said. Let’s make this conversation a foundation of kitten exams, and the better we do here, the more these cats will come back. A recent National Pet Owners Survey by the American Pet Products Association found that cat owners who see their veterinarian at least three times per year reported high use of flea and tick products. That’s better patient care, more educated and protected families, and increased revenue for the practice. It’s a win-win-win for everyone.

Scratching Post Training
Next on our list is another area that we often assume is known by every client and an automatic addition to a home with a new kitten, but often it’s an afterthought only when a behavioral issue arises. It’s always more effective to practice proactive, not reactive medicine. It’s also much easier for us to start with this basic recommendation and easy strategy for scratching post training from the very first visit.

Remember what we talked about earlier? Cat moms and dads often don’t know or recognize what NORMAL kitten behavior is, including the need to scratch. It’s our job to help educate them, in whatever ways are most efficient, that kittens explore their environment through scratching, and that should be expected!

Experts agree that there are four main reasons that kittens (and cats) scratch: to sharpen and remove old nails, to mark their area both visually and from an olfactory sense, to stretch after sleeping and to exercise their body[6]. And it

can become a very big problem if kittens are not trained from the beginning. A recent study by Moesta showed 83% of cats presented to a small animal practice demonstrated scratching of inappropriate items.

There are three key points to present to clients, especially those first-time pet parents who think adopting a kitten is as easy as putting down some food in a bowl a few times a week and leaving a litterbox somewhere in a closet! One, pet parents need to understand that kittens and cats love to live in vertical spaces FIRST and horizontal space second. It should not be a surprise to see kittens climbing, perching, jumping off high structures and loving to be up high. Two, the scratching posts should be placed in prominent social areas where that normal cat exploration is happening. Three, until a kitten settles in on a post, they should be offered different textures like cardboard, sisal, fabric, and others. In a nutshell, recommend multiple scratching posts first, using both vertical and horizontal spaces and varied textures so that kittens choose these when they are exploring their new home! And, for those clients who just want one suggestion, the S-shaped cardboard scratcher was most effective in a 2019 Zhang et al study[7].

We can't wait for this moment, because often, it's too late. The pet parent is already super frustrated, the bond is being worn down and the risk of relinquishment becomes much higher.

The Vaccine Experience

Let's shift gears a bit to what used to be the bread and butter of the kitten exams – the vaccines themselves. While they are still a core component, the shift must come from us to help meet our clients where they are: steering away from "giving a shot" to creating a vaccine experience while in our hospital.

That starts with the concept of "vaccine empathy". While many of us are back in person in our exam rooms with clients, some may still be curbside, and any pet parent that adopted during the pandemic didn't have the ability to witness this. They dropped off a kitten with a strange team member, usually talked to a veterinarian briefly on the phone, and then took home a sleepy, sore kitten with little explanation. While this was a necessity of veterinary pandemic survival, it did not help us build trust with the pet parents. Take time now to do things differently. Listen to client concerns, put yourself in their shoes and truly explain what is happening during and after vaccination. Remember, over 8 million pet parents today are in this for the very first time.

Part of these concerns often relate to human vaccine hesitancy and the concern about overvaccination. To help combat this, it's very important to not just change the exposure conversation about parasites, but also to be more intentional about exposures to infectious disease. Consider some of the following examples provided by the AAHA Feline Vaccination Task Force[8]:

- What is your kitten's typical day?
- How does your kitten encounter the outside world?
- Can you describe the environment your kitten explores outside?
- What type of supervision is on your cat's adventures?
- What other locations does your cat visit?
- Can you describe your cat's relationship with other pets and animals inside and outside your home?

Keep in mind, these don't have to be all verbally given in the exam room – these can be asked on pre-visit questionnaires, emails, and even as checklists on the website to help pet parents understand WHY vaccines are recommended with their individual family member.

We can't talk about vaccines without talking about handling. While so many of you are very familiar with low stress handling techniques, one thing we don't talk about much is what do we do if a kitten struggles with this at the first visit. A behaviorally normal kitten should be exploring, playing with toys, taking treats, and engaging with the veterinary team. If a kitten suddenly acts fearful, DON'T ignore this. Instead, this is where we offer specific tips about socialization and/or refer to a boarded veterinary behaviorist. No age is too young for referral.

The Purrfect Pedicure

Let's move some of our discussion to the education we will demonstrate in the exam room, but we want easy enough for clients to be able to do at home, starting with the Purrfect Pedicure.

One of the first things we need to teach, not only for reduction of bites and improved human-animal bond but also for recognition of what relaxed looks like, is how to read kitten body language. The continual challenge we face is educating pet owners how to recognize what their kitten or cat is communicating through body language. There is an easy starting point – the picture of relaxation. This is a kitten with a soft face, ears forward, beautiful almond-shaped pupils, the tail away from the body and relaxed muscle tone.

And, on the flip side, we have the “fractious” kitten or cat. These sweethearts get a bad reputation, often being labeled this in hospitals, but what we need to remember is these cats are predominantly scared, anxious, or both and rather than giving them a stigma, we need to give them space and help identify what triggers they have and how we can help them relax. Cats show reactive behavior through hissing, drawing back their lips, placing ears to the side or backwards, dilated pupils, tucked tail, crouched body and an arched back.

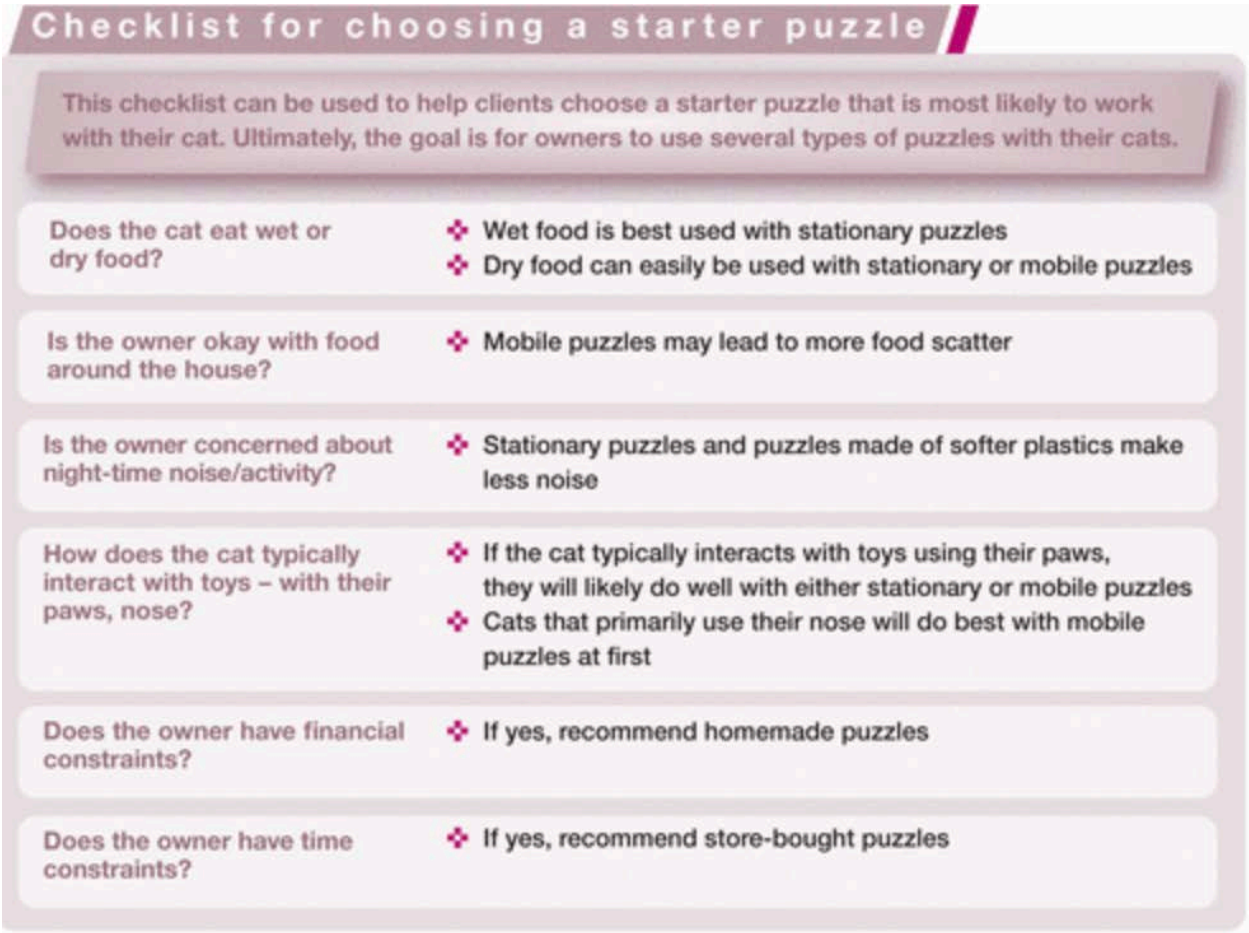
Besides understanding body language, let’s give pet parents some easy tips on how to prepare their kittens for nail trims for safety and help in scratching post training! Per the expertise of the late Dr. Sophia Yin, first, start with teaching pet parents to encourage kittens to lie on the back[9]. The kitten should be rewarded continuously and concurrently with yummy treats like Churu or small pieces of tuna on the end of a spoon. Once the kitten is comfortable with this position, shift to having paws and claws handled and gently squeezed. “When the paws are handled, treats should be given continuously at first, so the cat is just thinking about food.” (“Trim Your Cat's Nails Without the Stress - Vetstreet”) When paws are not being handled, stop any rewards.” The final step is to tap the nails and claws with a trimmer with the same treating method. If stressed body language is witnessed at any point, guide pet parents to stop, pause, and take a step backward until relaxed body posture is noted.

Throw Away the Food Bowl

Tip number six seems a bit bold but bear with me here! Give me just a few minutes to explain why kitten owners should ideally throw away their food bowls.

Well, what’s wrong with the bowl? In my mind, a lot of things! According to Dr. Liz Bales, cats spend 60-80 percent of their waking hours looking for prey. They have a need to hunt and catch their food, not be insulted by being given a bowl of food that could last for 3 days. When cats can hunt, they activate a pattern of “hunt, play, and kill”. This causes release of dopamine which Dr. Bales teaches it “heightens a cat’s arousal and triggers a feeling of happy anticipation rewarded by finding and eating the found food.” Equally important is the concept of FIC or FLUTD[10], depending on the camp you’re in. A recent study out of Norway demonstrated many different statistically significant risk factors for development of this multifactorial disease. Cats that were fed two meals a day out of a bowl had significantly higher risk as compared to controls that were fed ad libitum and those that had their food bowl in a less safe and comfortable location also were considered higher risk. Knowing this, let’s help start kittens off on the right paw with snackable portions encouraging the ‘hunt’.

One option for this style of feeding is food puzzles! If you’re new to food puzzle recommendations, I STRONGLY recommend downloading this journal article that is a comprehensive look at the why, the what, and the how. I find this checklist incredibly helpful for veterinarians, veterinary technicians, and even to link on websites or blogs. With as many choices as there are on the market, it can be overwhelming and even frustrating for well-intentioned cat parents. This can help narrow down our focus for more initial success.



Checklist for choosing a starter puzzle

This checklist can be used to help clients choose a starter puzzle that is most likely to work with their cat. Ultimately, the goal is for owners to use several types of puzzles with their cats.

Does the cat eat wet or dry food?	❖ Wet food is best used with stationary puzzles ❖ Dry food can easily be used with stationary or mobile puzzles
Is the owner okay with food around the house?	❖ Mobile puzzles may lead to more food scatter
Is the owner concerned about night-time noise/activity?	❖ Stationary puzzles and puzzles made of softer plastics make less noise
How does the cat typically interact with toys – with their paws, nose?	❖ If the cat typically interacts with toys using their paws, they will likely do well with either stationary or mobile puzzles ❖ Cats that primarily use their nose will do best with mobile puzzles at first
Does the owner have financial constraints?	❖ If yes, recommend homemade puzzles
Does the owner have time constraints?	❖ If yes, recommend store-bought puzzles

Dantas, Leticia MS, Delgado, Mikel M et al, Food Puzzles for cat: Feeding for physical and emotional wellbeing, *Journal of Feline Med and Surg,* Vol 18(9): 723-732.

Cat Carrier Coffee Table

Next on our list – redecorating! Ok, maybe that's a bit dramatic, but we need to set the stage from visit one that cat carrier training begins the moment the kitten joins the family, and the carrier becomes part of the furniture!

How does a cat carrier coffee table end up with us reaching our goal of kittens and cats LOVING their carrier? It's all about positive association and visual desensitization. Instead of being a trigger for kittens, it becomes the space they eat yummy food, receive relaxing pheromones, and are so comfy they want to nap[12]! It's a safe space and will continue to be for them. This is the number one piece of feline education that I kick myself about every day. I assumed every cat parent knew this stuff and did nothing to help lessen the very reason pet parents and cats are stressed about veterinary appointments. Make it a point to have everyone on your team on this mission.

Part of this training also includes helping everyone break bad habits, including ones we ALL do. Avoid that handle at all costs (even suggest duct taping it down!) and encourage everyone to carry cat carriers from underneath with two outstretched arms and a towel covering the top. This takes away the extremely bumpy ride that can cause motion sickness and anxiety around the item we've just spent months trying to create a positive association to at home.

These tips continue through the travel experience, but a few additional points to remember:

- Avoid honking, slamming doors, and minimize noise inside with low volume music
- Close the windows
- Avoid sudden starts/stops
- Keep carrier on the floorboard behind passenger side and/or secured in seatbelt
- Use pheromone sprays 30 minutes prior to travel in carrier and car

Enrichment from Day One

We're nearing the end of my list, but this topic still holds great weight. Bored kittens become mischievous kittens who become destructive cats when there is little to no enrichment in the home. Enrichment means emotional health and we know how critical this is to the prevention of behavior disorders.

Let's start with teaching kittens and pet parents how to play the RIGHT way. Do pet parents even know that's there's a wrong way? Do we as veterinary professionals? We need to teach a few key points. Toys, food puzzles, and interactive wands are a good way to go, and kittens demonstrating predatory sequences is totally normal and encouraged! However, let's be sure to strongly discourage play with our hands and feet and the super common internet recommendation of shouting "no" with a spritz from a water bottle. All that creates is fear and a diminished bond and the unwanted behavior will continue.

We also often assume that pet parents are completely in the know about litterbox husbandry, but you know what they say about assuming things… Don't take the chances I did and skip over this very important part of the visit: explaining how to set up a litter box properly at home. To start, if a kitten is not litter box trained at all, they should confine the kitten to a small room or have multiple litterboxes to choose. If the kitten has an accident, recommend using a food lure to encourage them to go back to the nearest box. Give guidelines on the size of the box (1 and ½ times the head to tail length as adult), that it should be uncovered, away from food and water bowls, and away from sounds and vibrations.

The other key part of enrichment? Thinking of a home's vertical space! Be proactive with the recommendation for cat trees and high safe spaces (preferably unique to each kitten). Encourage feeding yummy treats and placing comfy beds in these spaces to encourage exploration and teach families to respect these spaces as what they are – independent time for these family members.

One final quick tip? Keep using those smart phones! The more pet parents can take videos of normal behaviors (jumping, running, pouncing, etc.) when they have a kitten, the easier it can be to see differences indicative of possible pain and/or osteoarthritis later in life! Encourage pet parents to file these and save them for that possible rainy day down the road.

Send Them to School!
The second to last tip to launch kittens into a continuum for a lifetime of care is through hosting kitten kindergarten classes!

The idea of "Kitten Kindy Classes" was first developed by a leading veterinary behaviorist in Sydney, Australia, Dr. Kersti Seksel. The impetus for this program came after working with very frustrated owners over many years who were quite unaware of the differences between normal and abnormal cat behavior. Dr. Seksel unfortunately sometimes witnessed unresolvable situations in homes that led to relinquishments of cats which is devastating for all parties involved, including veterinarians. These classes are a solution to this by allowing veterinary teams to teach normal cat behavior help prevent behavior problems. As Dr. Seksel says, "We socialize and train kittens in these classes, but really it's for the OWNERS.[13]"

Now, before you say anything, I know this sounds amazing in theory, but NONE of us have any time these days! Keep this in mind. Successful kitten kindergarten classes are small (only up to 6 kittens) and only a TOTAL of three hours, period! The most important parts to emulate are to make sure the first visit is only with parents so that they aren't easily distracted! At the next two session, kittens will join, and we want them 8-12 weeks of age, have had their first vaccines and to finish before they are 14 weeks old.

Here's the other helpful piece – you really don't have to reinvent the wheel! Dr. Seksel provided topics for her three sessions to help guide this kindergarten journey[14]. In the first hour with just pet parents, it's important to discuss a cat's need for vertical spaces, how to create separate areas for eating, drinking, and sleeping, the essentials behind litterbox management, training, and enrichment ideas. When the parents come back the next hour for the second session, low-stress handling and socialization guidelines take center stage along with training tips and preventive health care strategies. In the final session, after learning all about normal cat behavior, the focus shifts to abnormal behaviors and disorders to allow early intervention and identification.

One bonus of these classes is the ability to incorporate teaching of practical moments in a kitten and cat's life. This could include how to administer oral meds and apply topical therapies[15], the proper fit and application of a leash and harness, brushing basics and reinforcement of the nail trim procedure. This also gives family members who couldn't be part of the first visit the opportunity to ask questions and meet the veterinary team.

Preparing For the Future
Finally, we need to prepare for the future. We've covered a lot of ground about how we can make the most of our time with kittens and their parents. Pick one, two, or all of these ideas and enhance the experience for everyone in

that exam room. That first impression is one of our best chances of seeing these kittens as adults and seniors consistently in life and having the trust of the pet parent for better partnership and compliance.

This unbelievable first kitten experience they have with you and your team creates an initial sense of community for these families. Continue your momentum that with these final tricks. Capture their next visit with forward booking and bond digitally with “Caturday” posts on your social platforms! Cat parents really love practices that have feline-specific hours, exam rooms, and even feline-focused products on their online pharmacy. Add to your website with feline-specific library resources and sections. And build community internally with Cat Friendly certifications for individuals or as a hospital. Knowledge is power, and community is empowerment. Let’s see more cats together!

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NOTES:

American Association of Feline Practitioners
2022 Spring into Feline Medicine ● April 24, May 4 & May 14

Feline Fracas: Why Cats Fight & How to Help Them

Theresa L. DePorter DVM, MRCVS, DECAWBM, DACVB

Introduction to feline fighting

Feline housemates don't always get along. Feline aggression may be active or passive. Feline fighting is a common reason for relinquishment. This session will review the complexities of feline social interactions and strategies for peaceful resolution of kitty controversies. Focus on understanding, managing and reducing aggression between housemate cats.

Social tension between housemate cats may manifest as overt aggressive encounters or passive avoidance of cats that live in the same home. The conflict may be obvious if cats are screaming or subtle if cats are simply avoiding interactions. While many cats form strong affiliative bonds with housemate cats, characterized by co-sleeping, nose-touching, and allogrooming, other cats forced to live together unwillingly may display a wide range of overt or passive aggression. Social conflict may begin when the cats are first introduced; or it may develop among cats that formerly had good affiliative bonds, either following a specific incident or due to gradual changes in the relationship. Overt displays of aggression include growling, hissing, screaming, spitting, attacking, chasing, and biting.[1] Passive displays include staring, blocking and hiding; some cats choose to run away or spend more time outside in order to avoid the conflict. Conflict between housemate cats may have elements of fear, anxiety, self-defense or territorial defense. Regardless of the underlying motivation and ethological cause, people don't like seeing their cats in distress; so conflict between housemate cats is a common cause of relinquishment. Other behavior consequences of social conflict may include urine retention, undesired elimination outside the litter box or urine marking.

According to the American Veterinary Medical Association (AVMA), there are 81.7 million owned cats in the U.S., versus 72 million owned dogs; and 35.4 million households own at least one cat. Cat-owning households have a mean of 2.1 cats, while dog-owning households have a mean of 1.6 dogs (American Pet Product Manufacturers Association, APPMA). Cat owners in the South keep more cats per household (3.2 cats) than any other region; compare New England (1.9 cats) and the Midwest (2.4 cats)[2]. Multiple cat households are common and keeping the peace is important for the emotional well-being of all cats in the home.

Development and pathophysiology of feline conflict

Cats have complex social relationships and aggression may be a normal behavior for independent felids. Between birth and three months of age kittens are rapidly developing their social skills and bonds: cats do progress through these critical periods of social interaction at earlier ages than dogs do. Appeasing pheromones are released naturally before and during this critical window suggesting a causal relationship or influence. Kittens prefer interactions with their queen but may accept grooming by a familiar adult cat (cross foster).[1] The socialization window for kittens begins at 2-3 weeks of age and then social malleability is rapidly decreasing as early as 8 weeks. Social encounters during this window will have dramatic influence on life long bonds with individuals and social skills in general. For example, kittens exposed to puppies or even rodents in this period are likely to be at ease with these species throughout their lifetime. Animal species or individuals not considered affiliative during this window of opportunity may always be considered a threat.

Social conflict and aggression is mediated by complex areas of the brain. It is believed that the hypothalamus and the amygdala are involved in aggression; specifically defensive aggression may be related to excitation of the ventromedial hypothalamus and amygdala. Intra species aggression may be mediated by the medial amygdaloid nucleus. Activation of the lateral hypothalamus is tightly involved in predatory aggression.[9,10] Aggression is a complex and often emotional issue with specific context, past experiences and personality can have an impact on the development and impulsivity of an individual fear-based response in each situation.[11]

Recognizing unhappy feline households

Cats may display conflict the first time they meet each other, or they may get along for years and then begin fighting. A single 'tragic event' can start a series of aggressive encounters that may persist long term or become more passive. Cats can become upset about a stray cat outside their home, or they can be startled by a sudden noise or distressed following a troubling car ride. If, at that exact moment, one cat locks eyes with another, an aggressive posture or fight may ensue. From that moment, the cats may not get along. Cats are poor at reconciliation. That is, cats lack the inherent skill to resolve a conflict, except by fighting or fleeing. Cats may be fixated in a stand-off, and neither cat has the skills to resolve the problem or just walk away. Cats don't reconcile well because cats don't generally offer appeasement gestures to resolve a social dilemma. If they are distressed or worried about an outcome, cats either flee or freeze. Other very social species, such as dogs, horses and people, have the social skill

set to “appease,” that is, a social skill package utilized to resolve differences. Cats are solitary and independent: tight social bonds with other cats in their social group are not essential. Cats are indeed social and may form close social bonds with some feline friends, but they are not dependent on those social relationships to survive. Cats have complex interactions and relationships, but they may not have a good reason to mend a soured relationship. Cats communicate by body language, so we may observe flattened ears, crouched body with the head low or a swishing tail. A defensive cat will hiss or scream. An aggressive cat may growl. Cats may display aloof disregard and avoid cats they dislike. Cats that are most comfortable together will sleep so close they are intertwined and groom each other around the head.

Management and Behavioral Modification Techniques

Once conflict has developed, complete or partial periods of segregation are helpful to maintain peace. Once the environment has been adjusted to provide a feeling of safety for both cats then behavior modification exercises may commence. Gradual reintroduction strategies and exposures must be carefully orchestrated to facilitate success and, more importantly, avoid setbacks.[5, 6] A successful outcome may be the accomplishment of “aloof disregard” rather than overt fighting.

Opportunities to explore the other cat’s living area may be beneficial, but only if the cats are calm during this scent exchange. Exposure to each cat’s scent when aroused or vigilant is likely counterproductive. Rotate each cat into the other cats living area to provide opportunities for exploration and scent deposition. Rotation sessions may occur for a few hours per day or a few hours per week. Avoid letting the cats see each other during these rotations. Keep affiliative pairs (dyads) together. The cats should be observed for signs of fear such as hissing, fleeing or crouching, indicating the process is too stressful. The cats should be observed for signs of stalking, arousal or vigilance. Rotations should be done without stress. The owner should be patient and avoid expedited reintroduction. In a successful rotation, the cats will not appear aroused and instead seem relaxed and oblivious to the scent of the other cats.

Practice calling both the aggressor and victims to a specific location in their separate areas for a treat. Practicing this until the cat comes reliably before attempting this cue in introductions may make them go more smoothly. It is important that the cat not be startled or reprimanded for failure to comply. Some cats can become acclimated using play therapy involving both cats. The cats can each play independently with an object while the other cat observes. Play may be initiated by the owner or the cat. Play should occur on each side of the doorway for cats too aggressive to be in the same room simultaneously.

The door way which separates the cats provides a zone of interaction which may be direct or passive. Provide treats, toys, catnip on either side of the door which separates the cats to create a zone of optional, surplus resources. Place feeding stations > 5 to 10 feet away from the door. The bowls do not need to be immediately adjacent to the door. Litter boxes should not be near this zone of interaction. The door may be modified to allow a viewing window or replaced with a screen door. This may allow too much visual interaction for cats with severe aggressive responses. Feliway® Friends* diffusers should be placed on each side of zone of interaction. *also marketed as Feliway® MultiCat in the US

Figure 1: Cats may be encouraged to play in the same area while still safely separated by doors by using toys. Photo courtesy of Theresa DePorter.

Semiochemical messages may be rotated. Surfaces that have been bunted by either cat may contain semiochemical communication. Provide scratching posts or “bunting combs” and then rotate these between each cats living area. A homemade bunting comb may be accomplished by putting a piece of cardboard extended through a doorjamb so the cats may rub on the edges that protrude on each side. The cardboard may be flipped in the doorjamb to provide an exchange of semiochemical messages. Passive exchange of each cats’ natural odors may be combined with pheromonatherapy. It is speculated that a common group odor contributes to harmony. Scent rotation is useful for

desensitization – passive exposure to each cats' scent without having to be exposed to the cat itself. If the cat is distressed about the smell of another cat then it is clearly too soon to introduce the cats directly. Use two wash cloths or hand towels (e.g. terry cloth, lamb's wool, dish cloth) and place one in each cat's preferred resting area for a few days. Rotate the cloths three times a week. The cats may be gently rubbed or stroked with the towels but I recommend avoiding vigorous or invasive rubbing which the cat may not like. Each cat should be calm and relaxed at the time the scent is collected. If the cat is worried or disturbed by the handling, then I worry that the shared chemical message may be one of distress rather than calm. I do recommend to also applying FELIWAY® Classic spray to each cloth before rotation. The cloth may be rotated several times a week. This passive scent exchange technique may be useful for cats living in different homes. Observe cats for any signs of distress, agitation or avoidance of the cat-scented and pheromone treated towel. Simply rotate bedding if the cats is easy to do and may be only option for cats that are too aroused by the scent collection process. A cloth should be left with each cat so it becomes familiar with the scent of the other cat(s). Cats should be observed for their reaction to the scent: if the cats become aroused, do not proceed to visual counterconditioning and desensitization exercises.

Reintroduction by active counterconditioning and desensitization: active exposure exercises may be useful but caution must be exercised to avoid causing distress. Patience is essential. Careful and close observation of signs of distress must be watched for closely. Tail swishing, dilating pupils or ears rotating to the side are all signs of feline conflict or distress. Overzealous exposures that result in aggressive displays may be extremely detrimental. The main goals should be on counterconditioning and desensitization exercises, *below* the threshold for either cat to react *and* to associate pleasant rewards when the other cat is present. The objective is to allow the cats to be together without causing any aggressive behaviors (growling, hissing, chasing, staring, etc.) and promote calm, relaxed behaviors in the presence of each other. The cats do not need to interact. If aggression occurs: do not startle, punish or reprimand. Introductions are best done slowly, and in a way that facilitates calm, non-anxious behavior (counterconditioning).The cats need to be far apart, so that they are relaxed (desensitization). Each cat is then offered a delectable food treat that they will eat but some cats will be uncomfortable eating with an aggressor in proximity. Object play may be more rewarding and successful if the cat is motivated to play. For safety and control, it is often advisable that each cat wear a harness and leash during introductions. Baby gates may be useful or doors may be modified with viewing windows or screens.

Psychopharmacology

Multimodal therapy including behavioral modification, environmental management, pheromones and medication is essential for successful treatment of cats displaying serious aggression or extreme aggressive displays.[5,6]
No medications are approved for use in cats for aggression; the following medication usages are extra-label. Owner consent forms are advisable. Administration strategies are crucial. Some medications may be hidden inside food or soft treats. Better to experiment with low-stress pilling techniques rather than to force-medicate the cat.

Serotoninergic medications (eg fluoxetine, clomipramine) are anxiolytics which may be given continuously on a long-term basis for chronic conditions and especially useful if the stress causing situations is unavoidable and there is prolonged exposure to trigger stimuli. Some serotonergic medications are specific for serotonin and others have effects on multiple neurotransmitters such as norepinephrine and dopamine. These medications are to be given on a daily schedule regardless of exposure to trigger stimuli. It may take > 4 weeks to achieve efficacy. In healthy animals, side effects from SSRIs and TCAs are usually mild, if they occur at all, and resolve within two weeks of initiating treatment. Other side effects include constipation, urinary retention, anorexia, gastrointestinal signs, tremors, irritability, and lethargy. Reduced appetite and sedation are the most common side effects noted by owners. The client should notice reduced reactivity and impulsivity after 4 to 6 weeks of continuous administration of an SSRI or TCA. Medications are to be continued for several months until the client has successfully completed the treatment regime and the pet has a new well-established, desirable behavioral response. Benzodiazepines may make cats friendlier and more outgoing, as well as have an increased appetite (helpful for behavior modification using food treats). But use with caution in animals exhibiting any level of aggression, as benzodiazepines may disinhibit aggression by reducing fear-based inhibition to biting. Gabapentin may be useful to reduce arousal and impulsivity in cats. All recommended doses are oral since transdermal doses have not been established, and poor absorption is a concern.

Recommended doses*.[5]

- Fluoxetine: 0.5–1.0 mg/kg PO q24h
- Paroxetine: 0.5–1.0 mg/kg PO q24h to 48h
- Clomipramine: 0.25–1 mg/kg PO q24h
- Buspirone: 0.5 – 1 mg/kg PO every 8h to 12h to 24h
    - NOTE: Buspirone should be prescribed for the victim only, as it may make the cat more outgoing and more overtly aggressive.

**full discussion of medications is beyond the scope of this paper. Consult formularies and individual drug monographs for complete details of indications, side effects, contraindications and precautions.*

Pheromonotherapy:

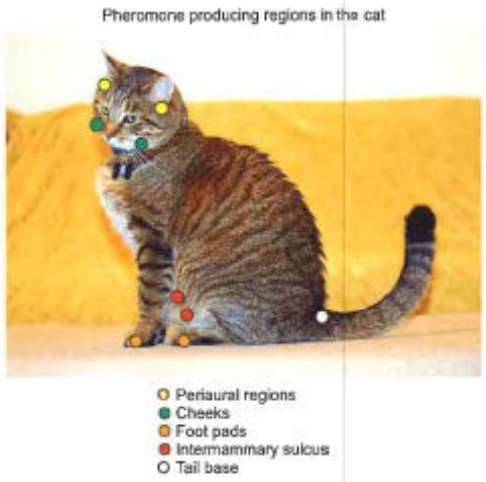
How to "defuse" Kitty conflicts with a pheromone diffuser. Pheromones are the most effective and benign option for reducing feline distress in some the cases. Cases involving extreme aggression cases will require a complex management approach and medication as described above. Cats should be provided the protective benefits of pheromones when faced with a stressful situation. Cats often communicate with other cats by leaving semiochemical messages, which are also called pheromones, in the environment, which other cats "read" in much the same way as people obtain information by reading a newspaper or book.[4] What if we could speak "cat"? What if we could write a message in cat language, send it to the cats, and influence their behavior? Pheromonatherapy is the art of leaving an encoded feline-friendly message in the environment by introducing a synthetic analogue of natural pheromones.[3]

Types of Pheromones

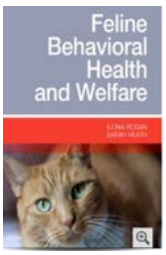
Pheromones may be useful preventatively or as a treatment for specific behavior problems. Five feline facial pheromones, designated F1 to F5, have been identified in cats. The F3 fraction is the pheromone deposited by the cat when facial-marking and chin-rubbing on either objects or people. This creates a familiar, comforting scent of "self" in the environment. The synthetic analogue of the F3 fraction is marketed under the trade name FELIWAY® Classic.

Appeasing pheromones, derived from the mammary area of mammals, have been identified.

Figure 2: Locations of natural pheromone sources in the feline. As shown in *Feline Behavioral Health and Welfare*. By Ilona Rodan and Sarah Heath. St. Louis: Elsevier, 2015. Courtesy of Theresa DePorter



Appeasing pheromones are released by the mother while nursing her offspring and serve to enhance bond formation while comforting and reassuring the neonates. Synthetic analogues of appeasing pheromones have been widely utilized in canines to reduce anxiety and promote feelings of comfort and well-being. ADAPTIL® (formerly D.A.P.) is a synthetic analogue of the canine-appeasing pheromone and has similar effects on older puppies and adult dogs. It has been effectively used to help puppies adapt to new homes; reduce fear and anxiety in puppy classes, the veterinary clinic, shelters, and during car travel; improve long-term socialization; and, in conjunction with behavior therapy, treat separation anxiety and noise phobias. Similarly, an appeasing pheromone of the cat is produced in the mammary sulcus of the queen. Ultimately it may be determined that a feline appeasing pheromone offers many benefits for cats just as the dog appeasing pheromone does for dogs. A new diffuser product called FELIWAY® Friends* is an appeasing pheromone which actually does not share any of the pheromones found in the similarly named feline facial pheromone product, marketed as FELIWAY ® Classic (formerly FELIWAY®), which most veterinarians are familiar with. FELIWAY ® Friends is ideal for reducing intercat aggression between housemate cats (http://www.feliway.com/uk/New-Feliway-Friends). Since the use of feline facial pheromone was first presented at the World Small Animal Association in 1996, FELIWAY® has become a household word for those that love cats.[7,8] Applications and benefits of Feliway have been well defined and it has been utilized to improve the wellbeing of more than 10 million cats from all around the world.



Research on feline appeasing pheromone use in feline conflicts.
The cat appeasing pheromone product, FELIWAY® Friends [also known as FELIWAY® MultiCat] by Ceva Santé Animale was evaluated for efficacy to reduce aggression between housemate cats by randomized double-blind placebo-controlled trial in 45 multi-cat households [appeasing pheromone (n=20), placebo (n=25)] that reported aggression for at least 2 weeks but much longer in most of the cases (average=822 days). Each household included 2-5 cats. Participants first attended a group enrollment meeting and the veterinary behaviorist described behaviors to be monitored for 7 weeks using the Oakland Feline Social Interaction Scale (OFSIS) which assessed the frequency and intensity of 12 aggressive interactions (e.g. bite, swat, stare, block, hiss or scream). Participants were provided directions for safely handling aggressive events. Punishment techniques were discouraged. Plug-in diffusers with FELIWAY® Friends or placebo were utilized for 28 days. Participants completed a daily diary of aggressive events and weekly social interaction scoring. Baseline scores were similar. The FELIWAY® Friends group showed a greater reduction in aggression score than placebo at day 7, 14, 21 and 28, which continued post treatment at days 35 and 42.[12] Cat appeasing pheromones appear to be a promising new treatment to reduce social tension among cats with a history of aggressive interactions.

Anecdotal reports during the clinical trial utilizing FELIWAY® Friends, I have been impressed by the enthusiasm people have for this new product and their observations about the effect on their cat's well-being:

- *"The cats are grooming each other. I haven't seen them do this for many weeks. The hissing and spitting has decreased. It's only been 6 days but already we can see a difference"*
- *"I noticed while the diffusers were plugged in, Suko was much more playful than usual, willing to play with cat toys she normally would ignore, and instigating playtime chasing and leaping with Cinnamon. Also, Suko was initiating cleaning Cinnamon more frequently and for longer periods of time without ending in biting, and the fights were cut in half and usually resolved quickly before the cats went back to playing or sleeping next to each other."*
- *"Dear Dr. DePorter, I've noticed regressions since unplugging the diffusers used for the aggression clinical study. Within a couple days after unplugging the diffusers, my eldest and youngest who are the trouble-makers, regressed to blocking, increased hissing, blocking and fighting that included chasing and smacking, staring and general intimidating behavior toward each other that was all present prior to beginning the study."*
- *"An interesting thing happened! One cat was resting in a bed and the other cat came into the room and jumped up to get on the bed. The cat accidentally landed on the cat that was resting. In the past this would have resulted in a major aggressive event including hissing, chasing, swatting and screaming. Instead they just hissed. I was very surprised! A very mild reaction compared to the screaming we would have heard in the past"*
- *"Lady Gray's hair is growing back. She has been an excessive groomer. She usually has thin hair on her legs but before the study she was bare on her belly, across hips and down her legs. Now her hair is growing back in! She seems less stressed"*
- *"We think Dash saw a cat outside. He chased Puzzle. Then he calmed down so quickly!! Even though an aggressive event happened, they recovered quickly."*
- *"The cats seem to be getting along better. Cats will lay in the same room without being mean to each other. Previously could not even be in the same room"*

In addition to the many families report to me that their cats experienced less social tension, characterized by an increase in the time the cats spent in relatively close proximity, more tolerance of agonistic displays, quicker recovery following encounters, and overall reduced tension.[13] Some families also report other changes in mood and social interaction with people. Some owners observed that the cats were more affectionate and interactive with human family members. The cats displayed more bunting and rubbing; they solicited attention more often, especially at bedtime; and they slept with family members more frequently and for longer periods.

When to use FELIWAY® Classic and when to use FELIWAY® Friends?
The FELIWAY® Classic formulation remains the most extensively tested and proven and utilized product which is beneficial for integrating a cat into a new home in contexts such as a new introduction, move, remodeling or common household stresses. FELIWAY® Classic remains the clear choice for cat displaying any urine marking. FELIWAY® Classic remains the first choice for facilitation of routine cat introductions but for situations which are likely to be more distressing, volatile and hold a higher risk for escalation and extreme cat-to-cat conflict problems then FELIWAY® Friends should be considered as an adjunctive therapy in combination with FELIWAY® Classic or, as a monotherapy for resolution of feline conflict.

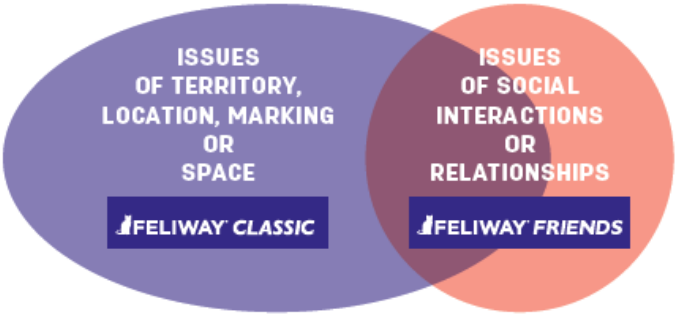


Figure 3: When to use FELIWAY® Classic or FELIWAY® Friends

Figure 4: When to use FELIWAY® Classic and when to use FELIWAY® Friends for kitty introductions

What constitutes a high risk situation for intercat aggression?
Cats may fight from the very first introduction or following a single incident involving stress. Other cats may change their interactions gradually over time. This may be influenced by many factors including the number of cats, their personalities and willingness to interact with other cats. The severity and intensity of the risk or occurrence of aggression will determine if FELIWAY® Classic will be sufficient to prevent or minimize a low intensity threat or if FELIWAY® Friends may be useful to alleviate conflict and arousal.

Practical considerations: how to apply a diffuser product advantageously
A pheromone diffuser works by warming a ceramic plate inside the diffuser and the pheromone contents of the vial are volatilized from the vial, by the wick and then released into the environment. This dense material will drift into the air and then settle on the nearby surfaces. Due to unique, species specific receptors in the vomeronasal organ only a cat is influenced by the feline pheromones but the cat has to be exposed to these pheromones. Pheromones are odourless; detectable scents are due to carrier fluids or other materials on the ceramic plate.

The ideal location for a pheromone diffuser is in a location the cat is noted sleeping and lounging often. Cats spend a considerable percentage of their time each day resting and are often consistent and very specific to the locations they select for resting. People know these locations – ask them where they would look for their cat. By putting a diffuser in the vicinity of preferred resting areas this increases the likelihood a cat will be exposed to an optimal dose. In multiple cat households, especially if there is conflict, it may be necessary to distribute diffusers so that each cat's preferred resting area is treated. Often cat parents will be focused on plugging the diffuser where cats fight or have conflicting encounters but this actually is not recommended as the cats may not get an adequate opportunity for exposure prior to an escalated state of arousal. Optimal placement would allow the cats to be exposed in advance of conflict with sufficient opportunity to be influenced by the appeasing message. The diffuser is plugged into an electrical outlet and the product is heated so the product is diffused through the cat's living environment. The diffuser must be oriented in the correct, upright orientation; the electronic portion should be on top and the liquid vial should be oriented below. Some air freshener units look similar but the bottle is on top so often clients will make this error without giving their decision conscious consideration. Slow diffusion may be due to an outlet that doesn't have electricity: some home outlets are on a wall switch and may be accidentally turned off. The diffuser should be placed in an open area which allows adequate space for diffusion. Avoid placing diffusers behind furniture, under tables or behind anything that may obscure the diffusion. Blockage will reduce the effectiveness of the product since the cat may not get sufficient exposure. Similarly open windows or strong air currents will scatter the pheromone and may reduce the overall effectiveness of the pheromone therapy. Dust or strong odors in the environment may settle on the ceramic plate in

the diffuser and then emit an odor when heated. This is generally transient. When not in use, the diffusers should be stored in the original package or other sealed container to prevent contamination which may result in an offensive odor when plugged in. The diffuser should be continuously plugged in and kept in the same location. The diffuser vials will last about 28 days and some variations may occur due to environmental variations in humidity, heat and air flow. The wick retains some liquid even when the diffuser bottle appears dry. The product also remains in the environment for a few days even after the refill vials are removed or appear empty.

Further, understanding the derivation and the natural applications of pheromones helps elucidate the appropriate applications and possible misapplications. If a cat is extremely terrified and simultaneously detects a semiochemical message conveying comfort and tranquility, one can imagine this may be more confusing or disconcerting to the feline psyche. In such a case, pheromones alone may be insufficient. Pheromone products are best applied to influence a behavioral response as they are not intended to completely control a specific response. For all behavior cases a thorough and careful analysis is best for optimal understanding of the behavior diagnosis and a comprehensive treatment program may be implemented. Even complex multimodal treatment programs may be augmented by a pheromone treatment which is safe and applicable to so many otherwise difficult problems in the cat-owning household. Use of a pheromone diffuser is a simple way to defuse volatile arguments between housemate cats.

Client Education

Clients must be willing to be patient. Resolution of aggression between housemate cats may require months of dedicated management, medications, pheromones and behavior modification, depending on the severity of the situation. Some cats may never get along. Premature introduction of fighting cats tends to prolong and exacerbate the problem. Caution is warranted anytime a cat leaves the home and returns (i.e. boarding, grooming or veterinary care) or during any stressful event. A single stressful event may result in an aggressive incident which may require months or years to resolve. The introduction of another cat to the home may further exacerbate social tension between familiar cats.

Steps for peaceful resolution of feline social tension*:

1. **Space.** Provide enough real estate for each cat to enjoy his/her preferred resting, playing and eating activities while still avoiding stressful encounters with housemate cats.
2. **Distribute important resources**. Each cat should have easy access to food, resting areas, scratching posts, toys and litter boxes without encountering an unfriendly cat.
3. **Meals**. **Cats should be fed separately.** Cats are not social eaters. Many fights or conflicts occur before or after mealtimes. Avoid a communal feeding routine. Feeding cats separately may reduce how quickly the cats eat and gulp their food. Eating in close proximity may contribute to social conflict and tension and may cause overeating.
4. **Don't force cats to interact.** Each time the cats experience an aggressive encounter, they are learning to fight next time. Patience is essential.
5. **Never punish or startle cats that are displaying aggression or fear**. No yelling, squirting or scaring. Cats may stop fighting and flee, but the overall tension will not be reduced.
6. **Guide cats to move away from an aggressive or tense encounter.** Encourage either cat to move away by using a sweet, gentle tone of voice. You may coax your cat using food, treats or toys. You may make noises that you know cause your cats to happily investigate (i.e., go to the kitchen and open a can of tuna).
7. **Pavlovian or classical conditioning.** You can change the cat's emotional association by pairing the presence of each cat with the occurrence of a desirable reward.
8. **Anxiolytic.** It may be necessary to reduce anxiety and distress with medications, pheromones or natural supplements.
9. **Health**. Be sure the cats are healthy and have been evaluated carefully for medical conditions Underlying pain or discomfort such as osteoarthritis or dental disease can contribute to irritability and social tension.
10. **Be realistic.** Some cats are not going to get along. Some cats will become friends. Some cats will achieve "aloof disregard" for each other.

*https://www.psychologytoday.com/blog/decoding-your-pet

Conclusions and implications

Consideration of the ethogram and social communication repertoire of affiliative behaviors in cats may provide prognostic or therapeutic information about the potential for reconciliation following aggression between familiar cats. Whether feuding dyads may be taught to reconcile or if the occurrence of reconciliative Behavior indicates successful stabilization of feline relationships should be the subject of further consideration and study. Use of pheromones, supplements and medication in severe cases to ease aggressions, arousal and reactivity may be useful to promote and enhance the feline reconciliation process.[5,6]

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NOTES:

American Association of Feline Practitioners
2022 Spring into Feline Medicine ● April 24, May 4 & May 14

Easy as One, Two, Pee: Steps for Solving Feline House-Soiling

Julia D Albright, MA, DVM, DACVB

Cats are one of the most successful species on the planet due to their ability to adapt to almost any environment, including indoor settings with humans. However, house soiling continues to be one of the most prevalent problems for cat owners and presenting complaints to veterinarians. Micturition and defecation are not just a means of removing the body of waste products, but also forms of social communication and a response to stress. Accurate diagnosis and an understanding of a cat's basic needs are crucial for treating out-of-the box elimination problems.

The motivations for a cat to eliminate outside of the box can be placed into two loose categories: 1) a need to void the bladder and colon but the provided litter box is unacceptable to the cat, or 2) a negative emotional state resulting in a desire to place urine or feces in a socially relevant location. Although terminology is not consistent in the literature, *unacceptable*/*inappropriate elimination* refers generally to urination or defecation outside of the box, regardless of the motivation. *Periuria* is, likewise, a general term for micturition outside litter boxes. *Toileting* refers to natural voiding behavior unrelated to marking, communicating social stress, or (usually) a disease state. Somatic medical conditions, such as lower urinary tract disease or gastrointestinal dysfunction, are often considered a third etiologic category, or a subcategory of toileting because the can create negative aversion or affect elimination urge. *Marking* behavior is depositing feces or urine for social communication, and *spraying* is a specific feline urine marking behavior in which the cat quivers the tail and sprays urine on a mostly vertical surface. The majority of this presentation will focus on feline toileting.

Toileting

Toileting can typically be identified by a cat urinating on horizontal surfaces and straightforward cases are often resolved by adjusting the litterbox environment to mimic natural preferences. Studies suggest that cats prefer:

Substrate

- *General* preference – clay clumping litter
- *General* dislike – synthetic materials like plastic beads, the substrate in most automatic cleaning boxes, pine pellets, baking soda additives
- Litter preferences vary and a simultaneous litterbox "cafeteria" –3-5 adjacent boxes each with a different litter substrates - is recommended to determine individual cat preferences
- Unscented recommended, but may not be major factor

Location

- Quiet but not necessarily visually isolated
- No corners or areas for cat to get trapped (e.g., corners) if social stress in the home
- Easy access (e.g., no stairs) if painful or frightened cat

Type of box

- Open, large, uncovered
- Low-sided if painful (osteoarthritis)
- No plastic liners

Number of boxes

- N + 1, where n = number of cats in the house (rule of thumb)
- If social problems among cats, spread boxes around house
- Cats sensitive to dirty box, multiple boxes in one location acceptable

Box Hygiene

- Scooping once daily and replacing litter q 2-4 weeks is generally acceptable but depends on number of cats and boxes
- Clean out box with mild soap or just water
- Some cats/households may need 2-3 cleanings/day, additional boxes, or automatically cleaning boxes (beware fear of noise, movement, aversive substrate)

Somatic diseases are common contributors to toileting. Pain or increased urgency can create a situation in which the cat cannot physically reach the designated litterbox, but also discomfort during elimination can also create a lasting aversion to the litterbox. Periuria can also be part of a larger sickness behavior complex. Over the last decade, mounting evidence links exposure to environmental stressors with signs of gastrointestinal, urinary tract, skin, respiratory, and other behavioral disorders. Based on these new findings, proper environmental enrichment such food- toy use, daily play, reward-based training, scent or food searching, and safe outdoor time (for some cats) should be "prescribed" for cats presenting for chronic sickness behaviors.

Marking

A cat spraying urine is suffering from social stress. The stress may be detection of a cat not associated with the social group (e.g., cat seen outside, scent of cat brought into the house on clothes or shoes), or friction between cats within a household. Avoidance through window film, blinds, or outdoor deterrents can be used for the former, but a more involved behavioral treatment plan that includes creating calm emotional responses is required to address discord within the home. Creating separate spaces, performing behavior modification, and therapies to alter chemical stress response and anxiety are common treatment steps in intercat aggression.

The diagnosis can become less clear when a cat is marking by depositing urine on a horizontal surface. A cat urinating on surfaces that are frequently used/worn by certain cats, dogs, or people indicate a social communication and stress displacement function.

Regardless of motivation for inappropriate elimination or species, previously soiled areas are more likely to become areas for future elimination. After removing the eliminations, it is recommended to clean the area with an enzymatic cleaner followed by an odor removing product. Cleaning the spot for several days by injecting cleaner into carpet and upholstery can help, but it can be difficult to completely remove the scent from thick fabric or subflooring.

The use of deterrents alone is not likely to be effective in treatment of inappropriate elimination. Remote activated deterrents that are not associated with people may be used in unacceptable, commonly soiled areas as long as the appropriate/preferred litterbox environment has been provided. Aversive smells and aluminum foil are not consistently effective.

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NOTES:

2022 Spring into Feline Medicine

THREE-DAY **VIRTUAL LIVE CE EVENT**

Sunday, April 24th | Wednesday, May 4th | Saturday, May 14th

ALL TIMES ARE EASTERN TIME ZONE

Sunday, April 24, 2022

TIME	SESSION TITLE	SPEAKER	SPONSOR
12:00 - 1:00 pm	Diagnostic & Therapeutic Approach to Feline URI	Dr. Mike Lappin	Boehringer Ingelheim
1:20 - 2:40 pm	Purrfecting Strategy & CommuniCATion in the FURst Kitten Visit	Dr. Natalie Marks	zoetis
3:00 - 4:20 pm	Feline Fracas: Why Cats Fight & How to Help Them	Dr. Theresa DePorter	
4:30 - 5:30 pm	Easy as One, Two, Pee: Steps for Solving Feline House-Soiling	Dr. Julia Albright	Purina Pro Plan Veterinary Diets

Wednesday, May 4, 2022

TIME	SESSION TITLE	SPEAKER	SPONSOR
2:00 - 3:00 pm	Diagnosis & Treatment of Proteinuria in Cats	Dr. Stacie Summers	Royal Canin
3:15 - 4:15 pm	Ionized Calcium in Cats: How Much are You Missing Without This Measurement?	Dr. Dennis Chew	zoetis
4:45 - 5:45 pm	Should You Extract This Tooth? Using Diagnostics to Decide (Probing, Intraoral Radiography, & CBCT)	Dr. Jan Bellows	Dechra
6:00 - 7:00 pm	Role of Dietary Phosphorus in Feline Renal Health & in Management of CKD	Dr. Stacie Summers	Royal Canin

Saturday, May 14, 2022

TIME	SESSION TITLE	SPEAKER	SPONSOR
12:00 - 1:20 pm	Hospice & Palliative Care: The Foundations for the Role of the GP	Dr. Mary Gardner	Lap of Love
1:40 - 2:40 pm	The Old Cat in the Clinic: How Senior Wellness Visits Improved Charlie's Quality of Life	Dr. Myles McKenna	zoetis
2:50 - 3:50 pm	The Itchy Cat	Dr. Mike Rossi	Ceva
4:00 - 5:00 pm	Frustrating Felines: Inappetant Cats	Dr. Diane Delmain	Purina Pro Plan Veterinary Diets

Diagnosis & Treatment of Proteinuria in Cats

Stacie Summers, DVM, PhD, DACVIM (SAIM)

Introduction

Proteinuria is defined as the presence of increased amounts of protein within the urine (>1.0 mg/dL). The type of protein can be any type and depends on the etiology of the proteinuria. Proteinuria can be classified as pre-renal, renal, or post-renal based on the etiology. Persistent renal proteinuria is of clinical importance and is defined as abnormal quantities of proteins in the urine that occurs secondary to disease in the renal tubules, glomeruli and/or interstitial space. Normally, proteins in the blood are prevented from being filtered into the urine by the glomerulus due to size and charge. Some small proteins may be able to pass the glomerulus and then are normally reabsorbed in the proximal tubule or broken down by tubular epithelial cells. When the glomeruli or tubules are damaged, excess proteins are filtered into and lost in the urine. Proteinuria is associated with the development of azotemia in cats more than 9 years of age, is an independent risk factor for disease progression in cats with chronic kidney disease (CKD) and is associated with a shorter survival time in CKD cats.[1-3] Because proteinuria is associated with negative outcomes in cats, it is important for veterinarians to diagnose and treat proteinuria in a targeted approach.

Steps in Proteinuria Workup

1. Screen for Proteinuria

The first-line test to screen for proteinuria is the urine dipstick performed as part of a complete urinalysis. Prior to classification of the proteinuria (i.e., pre-renal, renal, post-renal), veterinarians should confirm the persistence of the finding by rechecking a urinalysis with an inactive urine sediment at at least two time points in a stable patient. In some instances, documentation of proteinuria occurs in the presence of symptoms for hypoalbuminemia (peripheral edema, cavitary effusion) and in this scenario immediate evaluation and treatment may be necessary. In most cases, once the persistence of proteinuria is documented by urine dipstick, then the magnitude of the proteinuria should be documented with a urine protein-to-creatinine (UPC) ratio. The UPC ratio is a quantitative test to measure total urine protein. Based on the International Renal Interest Society (IRIS) guidelines, cats with renal proteinuria are identified as either non-proteinuric (UPC ratio < 0.2), borderline proteinuric (UPC ratio 0.2-0.4), or proteinuric (UPC ratio > 0.4).

The limit of detection of the urine dipstick is 30 mg/dL, and the test provides a semi-quantitative result (negative, trace, 1+ to 4+). The urine dipstick primarily detects albumin, therefore false negatives can occur with Bence-Jones proteinuria in cats with multiple myeloma. False negative can also occur if albuminuria is below the limit of detection and with dilute urine or acidic urine. False positives are common in cats, especially healthy cats with high urine specific gravities, and can also occur with alkaline urine. Sensitivity and specificity for the urine dipstick is as low as 60% and 11%, respectively, with the highest sensitivity and lowest specificity in healthy cats.

According to a recent study that compared urine dipstick to a UPC ratio, most cats with negative or trace proteinuria on urine dipstick did not have significant proteinuria (defined as UPC ratio >0.4).[4] Cats with a urine dipstick result of 1+ to 3+ had either a normal UPC ratio or significant proteinuria. All cats with a urine dipstick result of 4+ had proteinuria. In general, a UPC ratio should always be performed to detect and confirm proteinuria. However, in practice this may not always be feasible, and so the author considers the presence of an active urine sediment, urine dipstick result, urine specific gravity, age of the cat, and serum albumin (Figure 1) to aide in the decision in performing a UPC ratio. The following clinical scenarios support performing a UPC ratio: persistent proteinuria on urine dipstick, any cat with a urine dipstick 4+, cat with chronic kidney disease (IRIS substage) regardless of urine dipstick result, clinical suspicion for albumin loss (hypoalbuminemia).

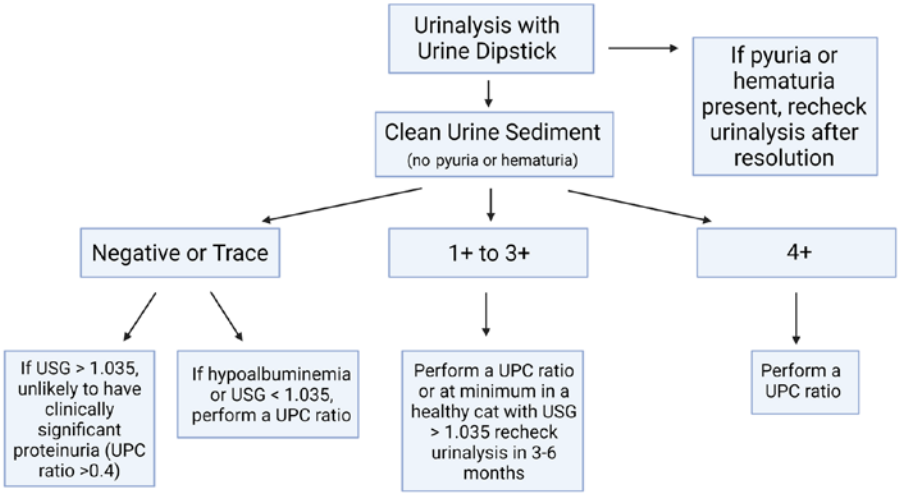

Figure 1. Flow chart for determining when to perform a urine protein-to-creatinine (UPC) ratio in a cat based on urine dipstick results.

2. Classify proteinuria and exclude pre- and post-renal proteinuria

After documentation of proteinuria, next step is to determine the origin of proteinuria and classify as pre-renal, renal, or post-renal in origin. First, exclude pre-renal and post-renal proteinuria, which can be done in most cases by performing a CBC, biochemistry panel, urinalysis, and blood pressure. In some cases, imaging of the urinary tract is needed (Table 1). Pre-renal proteinuria is generally mild and caused by increased amounts of proteins in the blood (i.e., overflow proteinuria) or a transient or persistent increase in renal blood flow (i.e., functional proteinuria). Post-renal proteinuria occurs with inflammation of the urinary tract. If a pre- or post-renal cause of proteinuria is found, correct the underlying etiology, and recheck a UPC ratio once resolved to determine persistence of proteinuria and potential underlying renal proteinuria.

Table 1. Classification and causes of proteinuria and diagnostic testing to consider in the evaluation of cats with proteinuria.

Causes	**Diagnostic Tests**
Pre-Renal Proteinuria	
Hemoglobinuria Myoglobinuria Immunoglobulin light chains	Complete blood count Biochemistry panel Visualization of the urine supernatant color Urine protein electrophoresis
Hypertension Seizures Fever Strenuous exercise	Indirect blood pressure measurement Body temperature
Post-Renal Proteinuria	
Urolithiasis Neoplasia Sterile cystitis Urinary tract infection	Urinalysis Urine culture Abdominal radiographs and/or ultrasound
Renal Proteinuria	
ICGN: Idiopathic Infectious (FeLV, FIV, FIP) Non-ICGN: Chronic kidney disease (IRIS stages 1-4) Acute kidney injury Glomerular sclerosis or atrophy Amyloidosis Polycystic kidney disease Renal dysplasia Renal lymphoma or other neoplasia	Serum creatinine and/or symmetric dimethylarginine (SDMA) with urine specific gravity Screening test for FeLV and FIV Abdominal ultrasound Renal histology with transmission electron microscopy and immunofluorescence

You may suspect renal proteinuria if the proteinuria is a persistent finding and you have excluded pre-renal and post-renal causes. In cases of renal proteinuria, proteinuria is caused by either damage to the glomeruli, tubules, or both. Damage to the glomerulus allows large (i.e., high molecular weight) negative charged proteins, like albumin, to be lost in the urine and can lead to severe proteinuria (UPC ratio >1.0) and hypoalbuminemia, which can manifest as nephrotic syndrome characterized by hyperlipidemia and ascites and/or peripheral edema. Damage to the tubules causes loss of low molecular weight proteins in the urine. A clinical suspicion of glomerular proteinuria is made in cases of high UPC ratio (>1.0) and/or hypoalbuminemia, however the absence of these findings does not exclude glomerular proteinuria. To definitively determine the origin or renal proteinuria, veterinarians can submit a urine sample urine protein electrophoresis test to determine the proportion of low, medium, and high molecular weight proteins in the urine.

3. Diagnose etiology of renal proteinuria

A renal biopsy that includes light microscopy with special stains, transmission electron microscopy, and immunofluorescence is needed to definitively diagnose the cause of renal proteinuria, however, is not indicated in a majority of cats with proteinuria. The most common cause of proteinuria in cats is CKD, which results in both glomerular and tubular proteinuria secondary to tubular atrophy and glomerulosclerosis. Importantly, tubular proteinuria can occur in cats with non-azotemic (IRIS stage 1) CKD which is consistent with tubular damage that occurs early in the disease process. Other causes of renal proteinuria include renal neoplasia and acute kidney injury secondary to hypoxic injury, toxin ingestion (ethylene glycol, lily), or pyelonephritis. Inherited renal disorders such as amyloidosis or polycystic kidney disease should be considered differentials for renal proteinuria based on signalment and imaging.

Immune-complex glomerulonephritis is an immune-mediated disease where immune-complexes deposit within the glomeruli of the kidney. The location of the immune-complex deposition varies and can occur in the glomerular basement membrane (membranous glomerulonephropathy), in the luminal surfaces of capillary walls (membranoproliferative glomerulonephritis), and mesangium (mesangioproliferative glomerulonephritis). Any inflammatory, neoplastic, or infectious disease can be a source of antigen that contributes to immune-complex formation. Cats with ICGN should be tested for infectious disease; in particular, retroviral infections. In a recent retrospective study, cats with ICGN had high UPC ratios (>2.0). In addition, a UPC ratio > 3.8 was both sensitive (91.9%) and specific (93.5%) for ICGN in cats.[5] In contrast to cats with CKD, cats with ICGN often suffer from hypoalbuminemia and can subsequently develop cavitary effusions or pitting edema.[6]

A renal biopsy in cats is performed under anesthesia. Only a biopsy of the renal cortex is needed, while avoiding the renal medulla to reduce the risk of bleeding. Given the narrow width of the cortex in cats, a surgical wedge biopsy of the renal cortex is often needed, however some skilled veterinarians may be able to perform an ultrasound-guided tru-cut biopsy of the cortex. Renal tissue should be submitted for three tests: light microscopy with special stains (e.g., Congo red), transmission electron microscopy, and immunofluorescence. ICGN cannot be excluded without transmission electron microscopy and immunofluorescence. More information on how to perform a renal biopsy, obtain a renal biopsy kit, and submission of the renal biopsy can be found online on the International Veterinary Renal Pathology Service (IVRPS) website (https://vet.osu.edu/vmc/international-veterinary-renal-pathology-service-ivrps).

The benefits and risk of performing a renal biopsy should be considered for each patient. Prior to renal biopsy, review of past medical history, feline retrovirus testing, and abdominal ultrasound to evaluate renal morphology is indicated. In addition, the safety of performing a renal biopsy should be assessed. Contraindications to renal biopsy include uncontrolled hypertension, bleeding disorder, end-stage CKD, polycystic kidney disease, hydronephrosis, and moderate to severe anemia. Veterinarians might consider a renal biopsy when there is persistent subclinical renal proteinuria that is unresponsive to treatment, severe proteinuria (UPC ratio >3.5), hypoalbuminemia secondary to proteinuria, presence of nephrotic syndrome, Abyssinian with proteinuria to confirm amyloidosis, progressive proteinuria, and prior to immunosuppression for treatment of ICGN. Overall complication rate of renal biopsy in cats is 18.5% with severe hemorrhage the most common type of complication.[7]

Treatment of Renal Proteinuria

Goal of treatment is to reduce UPC ratio to less than 0.5 or by greater than 50% and resolve hypoalbuminemia (albumin >2.5 g/dL) if present. Treatment of proteinuria includes dietary protein restriction, renin-angiotensin-aldosterone system (RAAS) inhibition, and, in cats with ICGN, immunosuppression.

The mainstay of treatment for proteinuria is a reduction in dietary protein intake while maintaining normal caloric intake. Dietary protein restriction has been shown to reduce proteinuria within 1 month in dogs, and the same is believed to be true for cats.[8] Protein restriction is recommended in cats with significant persistent renal proteinuria, even those without azotemia. However, the degree of protein restriction will depend on the cat's current protein

intake and degree of azotemia (if present). It is critical to avoid excessive dietary protein restriction. In general, reduce total dietary protein intake by 25-50% depending on severity of proteinuria, azotemia, and clinical signs. A more conservative reduction might be considered if the cat's current diet has a protein concentration near the AAFCO minimum for cats (26% ME). Therapeutic kidney diets formulated for cats vary in protein concentration (21-31% ME) and may not be necessary unless advanced stage disease (IRIS stage 3 or higher) or hyperphosphatemia is present. An omega-3 fatty acid supplement may be beneficial in cats with proteinuria due to its antithrombotic and anti-inflammatory effects. A dose of 40 mg/kg EPA and 25 mg/kg DHA is recommended.

The use of angiotensin receptor blockers or ace inhibitors are commonly used for treatment of renal proteinuria. They are effective at reducing the magnitude of proteinuria by dilating the efferent arteriole in the glomerulus of the kidney, therefore reducing glomerular pressure and filtration rate. While both classes of drugs inhibit RAAS, they do so by different mechanisms. Ace inhibitors, such as benazepril, inhibit the ace enzyme that converts angiotensin I to angiotensin II. Telmisartan, an angiotensin receptor blocker most used in veterinary medicine, specifically inhibits the angiotensin II type-1 receptors. The starting dose and dose increase strategy for benazepril and telmisartan is found in Table 2. The author's preference for RAAS inhibition for treatment of proteinuria is telmisartan based on studies in cats and dogs.[9,10] After starting RAAS inhibition or after a dose change, renal function and blood pressure should be assessed within 7 days and 4-6 weeks, along with a urinalysis and UPC ratio. If therapeutic goal has not been met by 4-6 weeks, the dose is increased, and similar monitoring is performed. An increase in creatinine concentration more than 30%, hyperkalemia (>6.5 mg/dL), or hypotension warrants discontinuation and instituting the drug at a lower dose or consider further diagnostics (e.g., renal biopsy, if indicated).

Table 2. The starting dose and dose increase strategy for benazepril and telmisartan in cats.

Drug	Starting Dose	Dose Increase Strategy
Benazepril	0.25-0.5 mg/kg PO per day	Increase by 0.25-0.5 mg/kg to max daily dose of 2 mg/kg
Telmisartan	0.5-1.0 mg/kg PO per day	Increase dose by 0.5 mg/kg to max daily dose of 2 mg/kg

In those cats with a biopsy confirmed diagnosis of ICGN, immunosuppression is indicated. The preferred drug is mycophenolate at dose of 8-10 mg/kg PO twice daily. Veterinarians may consider a short 7-day tapering course of prednisone in those cats with severe clinical disease. Mycophenolate should be continued for 8-12 weeks before changing course of treatment with monitoring of kidney function, urinalysis, and UPC ratio every 2-4 weeks. The most common side effect in cats receiving mycophenolate is dose-dependent gastrointestinal signs, particularly diarrhea. Cats with ICGN that received mycophenolate had longer mean survival time (244 days) than cats that did not (17 days).[6]

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NOTES:

American Association of Feline Practitioners
2022 Spring into Feline Medicine ● April 24, May 4 & May 14

Ionized Calcium in Cats: How Much are You Missing Without This Measurement?

Dennis J. Chew, DVM, DACVIM (Internal Medicine)

DETERMINATION OF CALCIUM STATUS

Q: How common is hypercalcemia in cats?
A: Hypercalcemia is most often defined in primary care practice initially by the finding of increased serum total calcium on routine serum biochemistry. The overall frequency of hypercalcemia is less common in cats than that encountered in dogs but the frequency of finding hypercalcemia in cats has dramatically increased in many regions of the world over the past 20 years mostly due to the diagnosis of idiopathic hypercalcemia (IHC). Mild hypercalcemia based on serum total calcium is often overlooked (often thought to be due to hemoconcentration from mild dehydration) during analysis of serum biochemical profiles so it is likely to be more common than generally appreciated. When screening cats for calcium status using ionized calcium instead of total serum calcium, hypercalcemia was found with greater frequency (Schenck Can Vet 2010).

Q: I keep hearing that it is "better" to measure ionized calcium instead of total calcium. Is that true, and why if so?
A: YES, it is true since ionized calcium is the biologically active form of calcium. If the clinician only evaluates total serum calcium, many cats with a normal total calcium will have an ionized hypercalcemia that will be missed. In dogs, the finding of a high total serum calcium tends to over-predict how many dogs will have a parallel increase in ionized calcium, especially dogs with CKD; this does not happen with much frequency in the cat. The only way to know the true calcium status for sure is to measure ionized calcium.

Q: Why is it that so many of my colleagues are now measuring ionized calcium in both dogs and cats? I thought that was difficult to do and too expensive for my clients.
A: It used to be considerably more difficult and expensive to measure ionized calcium as it required sending samples to reference laboratories following special anaerobic handling conditions. This limited the veterinary community's enthusiasm to measure ionized calcium. The development of in-house point of care analyzers like the i-Stat® has revolutionized measurement of ionized calcium in private practices that can be done in house without special handling of samples and results are generated accurately, rapidly, and affordably.

Q: How important are pre-analytical considerations when measuring ionized calcium using a point of care instrument?
A: They are quite important in order to generate accurate and reproducible results. Whole blood anticoagulated with lithium heparin is the usual sample analyzed. It is important to fill the regular size (1.3 mL) tube to the same fill volume line (0.5, 0.75 or 1.0 mL) each time in order to have the same dilutional effect of heparin in the sample. Microtainer tubes should be filled to the 0.2 or 0.4 mL mark. Microtainer tubes are especially attractive for use in cats due to the smaller volumes needed. Tubes should be well-mixed multiple times before the whole blood sample is inserted into the instrument cartridge. Care should be taken to limit exposure to room air that could alter the pH of the sample during loss of pCO_2 and change the ionized calcium results.

Q: Should I "correct" total calcium based on albumin or total protein?
A: No. There may be some value in those with hypoalbuminemia to see what the "corrected" calcium would be in the face of normal proteins. The "corrected" total calcium does not generally improve alignment with ionized calcium at the same time (Schenck 2010).

Q: Should I predict ionized calcium using total serum calcium?
A: Most cats with and without CKD and a total serum calcium > 11.8 mg/dL were found to also have an increase in ionized calcium. However, quite a few cats with a normal reference range total serum calcium were found with high ionized calcium in the same study (van den Broek 2017). There was substantial discordance in characterizing hypercalcemia in cats by ionized calcium vs total calcium in another study (Schenck 2010).

Q: Should I predict ionized calcium using total serum calcium and a series of other routine biochemical analytes in cats?
A: In the absence of ability to measure ionized calcium, this estimate could be helpful, but no surrogate is as good as actually measuring ionized calcium directly. Predicted ionized calcium using multiple variables was highly specific but poorly sensitive in cats with hypercalcemia and hypocalcemia in one study (Hodgson 2019).

Q: Should the reference range for total and ionized calcium be expanded so that we don't have to deal with seemingly "trivial" increases in calcium?

A: This is not a good idea. The reference interval already appears to be expanding some from what I can tell, possibly by the inclusion of those with IHC into the so-called group of "normal" cats. It is better to know sooner, rather than later, when calcium is creeping out of range.

Q: Must I measure ionized calcium?
A: YES, if you really want to know what is going on regarding calcium status with great certainty.

Causes/Differential Diagnosis of Hypercalcemia in Cats
Q: What major organ system(s) is resonsible for the generation of hypercalcemia in IHC cats?
A: We do not know how this type of hypercalcemia is generated. It could result from enhanced resorption of calcium from bone, enhanced GI absorption of calcium, impaired renal excretion of calcium, or some combination of these mechanisms.

Q: What are the most common causes or associations for hypercalcemia in cats?
A: IHC is the most common cause for hypercalcemia discovered in primary care practices, followed by cats with CKD, and then those with malignancy associated hypercalcemia. Primary hyperparathyroidism follows as next in likelihood.

Q: I just discovered a 12.8 mg/dl total calcium (10.2 mg/dl is upper limit of reference range for my laboratory) on blood test results taken during a wellness exam from what I thought was a healthy middle-aged cat. All of the other biochemical tests were normal as was the CBC. How concerned should I be that this cat has malignancy- associated hypercalcemia (MAH)?
A: We are always concerned about the possibility for malignancy as the cause of hypercalcemia in both dogs and cats, but MAH is much less common in the cat compared to the dog (it is the number one cause of pathological hypercalcemia in the dog). Based on serum total calcium, malignancy associated hypercalcemia (MAH) is 3rd in frequency behind IHC and CKD. Patients with MAH are usually "sick" as it takes a reasonably large tumor burden to synthesize the molecules (especially PTHrP) that result in hypercalcemia. So it seems unlikely for this cat to have MAH, especially when the hypercalcemia persists for a longer period of time without the cat showing more clinical signs. The less sick the cat is in the face of persistent hypercalcemia, the more the likelihood for the diagnosis to be that of IHC or primary hyperparathryodism. Remember, ionized calcium should always be performed first to confirm the diagnosis of clinically-relevant hypercalcemia.

Q: How do I know if this cat really has IHC?
A: The diagnosis of IHC is one of exclusion after initially confirming that the ionized calcium is increased. All the known causes of hypercalcemia should ideally be eliminated – but this kind of workup can be exhaustive and expensive. The ionized calcium must be increased, by definiton. Step one in patients with ionized hypercalcemia is to measure PTH to determine if the process is PTH-dependent (high PTH from abnormal parathyroid glands) or PTH-independent (PTH is suppressed from response of normal parathyroid glands). Compared to dogs, cats have a higher frequency of PTH-independent hypercalcemia. In those with parathyroid-independent hypercaclemia, the next step in the diagnostic evaluation is to rule out MAH which requires imaging of the thorax and abdomen. Abdominal ultrasonography is also helpful. The typical pattern for calcium regulatory hormones in IHC would be for PTH concentration to be within the reference range (often lower end to zero), PTHrP undetectable, and normal serum iMg. 25-hydroxyvitamin D and calcitriol concentrations are usually in the reference range.

Q: What clinical signs should a cat with IHC display?
A: About 50% of cats with IHC have no obvious clinical signs that are noted from owners and their veterinarians during submission of samples to endocrinology laboratories. In many instances, hypercalcemia based on total serum calcium evaluation is fortuitously discovered following submission of samples from wellness examinations or pre-anestheic evaluation of seemingly healthy individuals. Hypercalcemia is also sometimes discovered following submission of samples from cats with seemingly trivial clinical complaints like intermittent vomiting. History can include mild weight loss, a diagnosis of inflammatory bowel disease, chronic constipation, vomiting, and anorexia. GI signs may be attributed to the aderse effects of ionized calcemia on gut motility. Uroliths have been reported in about 15% of cats with IHC; calcium oxalate stones were specifically noted in 2/3 of these cats.

Q: I believe I have a cat with IHC. The owner's were willing to analyze PTH and ionized calcium but are reluctant to go further with my recommendations of more blood work, radiographs, and ultrasound to make an air tight diagnosis of IHC. What is the least amount of diagnostic workup I can do and still feel secure about the diagnosis and starting treatment?
A: Yes, it is true that full imaging with thoracic and abdominal radiographs along with abdominal ultrasound is the gold standard in the diagnosis of IHC. Many clients will not pay for the gold standard diagnostic evaluation. Lack of

clinical signs in conjunction with low PTH and ionized hypercalcemia significantly increases suspicion of IHC. In this case, it may be appropriate to presumptively diagnose IHC.

Q: Can a cat with CKD also have IHC?
A: YES in my opinion. Others believe that since there is an underlying diagnosis of CKD, the hypercalcemia does not qualify to be idiopathic. This is tricky if one does not know the circualting PTH status. In usual cases of CKD without hypercalcemia, PTH is often times above the reference interval or at least in the upper half of that range. In those with IHC and CKD the PTH is usually zero or very close to it. In the original case series describing IHC in cats, some had hyperclacemia first followed by development of azotemia, others had azotemia first and then hypercalcemia developed, and the last group had both azotemia and hypercalcemia discovered at the same time. Given the new knowledge about early CKD in cats and the emergence of hypercalcemia while eating renal diets moderately restircted in phosphate content (see Q later regarding diet and diet treatment), it is conceivable that this diet induced hypercalcemia and then suppresssed PTH to near zero. In some instances where there is enough serial biochemical data, the time line for emergence of hypercalcemia first and then azotemia supports that the CKD was created or progression enhanced by the IHC.

Q: Someone told me that Bartonella infection is associated with IHC in cats. Is this true?
A: No association has been found between positive serlogy for Bartonella and for IHC (Whittemore 2014). It is possible that Bartonella-associated infection and granulomatous inflammation could create hypercalcemia related to synthesis of 1,25(OH)2vitmain D in an unregulated manner by activated macrophages.

DIAGNOSTICS
Q: What is the minimal diagnostic workup that I must perform and analyze before I can arrive at the diagnosis of IHC with great certainty?
A: Traditionally, this has been based on measurement of an ionized calcium with PTH determination on the same sample. Ionized calcium has to be high by definition, and PTH must be within the reference range, preferrably reduced to the lower 1/3 of this range. Chest radiographs and some combination of abdominal ultrasonography or radiography needs to be performed in order to exclude organomegaly or masses that could arise from malignancy or granulomatous inflammation. This “minimal” workup will miss some cats that have underlying hypervitaminosis D, so we recommend that measurement of 25(OH)-vitamin D be added to ionized calcium and PTH on the same sample.

Q: How variable is the concentration of circulating ionized calcium in the same cat with IHC over time?
A: Surprisingly, this had not been studied. We do know of some IHC cats in which the measured ionized calcium varies to within and above the reference range at different hospital visits. Studies need to be designed to measure ionized calcium over the hours of the day, daily, and weekly so that the variability of ionized caclium can be measured in IHC cats. There is minimal variation in circulating ionized calcium concentrations in normal cats.

Q: Is it more likely for ionized calcium to vary from above to within the reference range early on, or later, in the IHC disease process?
A: In IHC cats with minimal increases in ionized calcium, it is more likely to identify instances in which the ionized calcium will be found to fluctuate within and above the reference range. It is less likely that IHC cats with more severe increases in ionzed calcium will enter the reference range but the degree of variation in this subset of IHC cats has not been studied for this variability.

Q: Do you believe that PTH reported as 0 in many cats with IHC is possible?
A: PTH often returns from endocrinology labs as 0 in cats with IHC. Traditionally, there is a non-suppressible component of PTH in the face of ionized hypercalcemia, leaving some PTH to be measured. The assay used to measure feline PTH is adapted from one designed to measure human PTH so it is quite possible that we are not really measuring all the feline PTH that is there. Alternatively, high circulating levels of ionized calcium completely shut down the release of PTH. We really need a PTH assay in which synthetic feline PTH has been used to determine the sensitivity of the human assay kit to measure feline PTH.

Q: What happens to the calcium regulatory hormones after ionized calcium has been returned to normal during treatment?
A: Unfortunately, calcium regulatory hormones (PTH, 25D, 1,25D) have only been measured as part of the diagnostic process before starting treatment. Measurements of this nature following treatment are likely to shed further light onto the underlying pathophysiology of IHC.

Q: Is IHC likely to be one disease?
A: Probably NOT. We have not been able to show that it is a primary endocrine disorder, but it has secondary endocrine responses that can be appropriate or abnormal. It could be a dietary sensitive or nutrient senstive disease

for some cats. There are some autoimmune diseases that affect the function of the Vitamin D receptor (VDR) and the calcium-sensing receptor (CaR) that could be operative in cats with IHC. Genetic mutations in the pathways for vitmain D metabolite activation and inactivation could also result in hypercalcemia. It appears llikely that genetic susceptibllity/vulnerability allows some cats to develop IHC when exposed to provocateurs.

Q: Concentrations of 1,25(OH)2-vitamin D (calcitriol) are within the reference range for most cats with IHC (a few do have concentrations above the reference range). Should calcitriol concentrations be suppressed to low levels in the face of ionized hypercalcemia?
A: YES. The finding of "normal" reference range calcitiol concentrations is not usually considered to be "appropriate" in the face of ionized hypercalcemia. High levels of ionized calcium are expected to supress the activity of renal 1-alpha-hydroxylase so that less calcitriol is synthesized. It is possible that something associated with IHC is altering the ability of this enzyme system to respond appropriately to the ionized hypercalcemia. It is possible that seemingly "normal" circulating calcitriol could be contributing to the genesis or maintenance of ionized hypercalcemia.

Q: Concentrations of 25(OH)2-vitamin D (calcidiol) are within the reference range for most cats with IHC. Should calcidiol concentrations be suppressed to low levels in the face of ionized hypercalcemia?
A: No. Ionized calcium concentrations do not directly regulate how much vitamin D is converted to 25(OH)-vitamin D. Circulating 25D mostly reflects dietary vitamin D intake and its absorption into the circulation, as D is rapidly converted to 25D within the liver in a largely unregulated manner. Interestingly, there is a subgroup of IHC cats that have low 25 levels for reasons that are not clear. Those with increased circulating 1,25D may suppress vitmain D conversion to 25D.

Q: Do you believe the reported reference ranges for circulating 25D levels in normal cats?
A: The reference range for normal cats has been established in cats eating foods that are supplemented with vitamin D to varying degrees.The 25D reference range is very wide reflecting the great variability in the amount of vitamin D supplemented in various foods, and biological variablilty in absorption of vitmain D and its conversion to 25D within the liver. Our suspicion is that commercial foods are supplemented with abundant vitamin D in an attempt to avoid development of deficiency. It is possible that IHC cats are more sensitive to "normal" concentrations of circulating 25D. It would be very interesting, and perhaps informative, to know the vitamin D status of cats living in the wild that do not consume human foods or grocery cat foods.

Q: Should high-frequency ultrasonography of the parathyroid and thyroid glands be part of the routine workup for cats supected to have IHC?
A: No, unless there is concern about a diagosis of primary hyperparathyroidism. It would, however, be good to have this information as part of trying to figure more out about the pathophysiology of IHC. In cats with PTH that is not suppressed to the lower 1/3 of the reference range in the face of ionized hypercalcemia, we do recommend to image the parathyroid glands to see if they are enlarged.

Q: Should ACTH cortisol stimulation testing to exclude hypoadrenocorticism be part of the routine workup for cats with IHC?
A: Hypoadrenocorticism in cats can cause hypercalcemia, but these cats are usually severely ill with a combination of hypercalcemia, hyponatremia, and hyperkalemia. Hypoadrenocorticism causing hypercalcemia in the absence of changes in serum sodium and potassium has not been reported in cats, but this phenomenon has been suspected to occur in dogs (Joe Bartges personal communication). To make the most iron-clad diagnosis of IHC, ACTH cortisol stimulation testing could be done to exclude hypoadrenocorticism. Few cats with IHC have ever been tested for the possiblity of underlying hypoadrenocorticism. Reduced adrenal reserve (low post ACTH cortisol) has been observed in cats with interstitial cystits without any changes in serum electrolytes. It is possible that reduced adrenal function could contribute to the development of IHC in cats.

Q: Should bone marrow cytology/biopsy be performed to exclude malignancy of the bone marrow as part of the routine workup for cats with hypercalcemia?
A: No, if the cat is otherwise relatively healthy. YES if the cat is quite ill and has some type of cytopenia – neutopenia, anemia, thrombocytopenia to suggest bone marrow involvement. The chances of establishing a diagnosis of a bone marrow disorder capable of causing hypercalcemia otherwise is exceedingly low. An exception would be to aspirate osteolytic bone lesions detected on imaging to exclude cancer or granulomatous inflammation.

Q: Is there any relationship between hyperthyroidism and IHC in cats? Should T_4 be measured as part of the routine workup for cats suspected to have IHC?
A: Hyperthyroidism is usually associated with normal to low circulating calcium status in cats. Hyperthyroidism is known to be associated with increased bone turnover in people, so it is possible that hyperthyroidism could result in

hypercalcemia if kidney function is compromised. We have observed ionized hypercalcemia in a few cats with hyperthyroidism that resolved following treatment with I-131.

Q: Does aluminum accumulation in the body have any role in the development of hypercalcemia?
A: We do not know for sure, but aluminum is known to accumulate during CKD and could contribute to the development of ionized hypercalcemia (human, dog). Aluminium accumulation in bone can prevent deposition of calcium into bone, so the balance between calcium deposition and resorption is disturbed. This could be an underlying mechanism for development of ionized hypercalcemia in CKD cats that have been receiving aluminum containing intestinal phosphate binders for a long time.

TREATMENT

Q: Do I really need to treat IHC? This cat doesn't seem to know it has IHC. What bad things could happen if I don't treat the IHC?
A: Though many cats with IHC do not have obvious clinical signs at first look, a more careful review of the history and physical examination often discloses some abnormality that could be explained by persistence of chronic ionized hypercaclemia. This includes low-grade weight loss, loss of muscle mass, and lethargy. Intermittent vomiting and constipation are also possible. Chronic ionized hypercalcemia is a risk factor for the genesis of calcium oxalate urolithiasis and for the development of chronic renal injury resulting in CKD – this may take months to years to develop.

Q: What is the best treatment for stable IHC in cats?
A: The ideal treatment would be to remove the underlying cause for the hypercalcemia, but this is not possible because the pathogenesis for IHC remains unknown. Some combination of dietary change, oral prednisolone, or oral bisphosphonate (alendronate) is usually recommended. In our practice, oral alendronate has often been the treatment choice for IHC that is most likely to result in long term restoration of normocalcemia (see other questions below). This standard of care is changing, as we are starting to understand how to better prescribe effective dietary modification that restores normocalcemia. Long term alendronate treatment can result in adverse effects on bone (see Q later).

DIET AND DIETARY CHANGE

Q: I have heard that a dietary change to a higher fiber diet works to restore normocalcemia in cats with IHC- do you agree, and which diet would you recommend if so?
A: The feeding of increased dietary fiber decreased serum calcium in some cats (McClain 1999) but not in others (Midkiff 2000). Higher fiber diets may decrease intestinal absorption of calcium due to decreased transit time, but the effects of fiber are considered complex since fiber also tends to decrease colonic pH leading to ionization of calcium, thus increasing its absorption. Types and amounts of fiber present may also affect calcium control. These “high fiber diets” are supplemented with higher concentrations of calcium compared to maintenance diets. Therefore, calcium content is not the reason for the decrease in circulating calcium sometimes achieved on these diets. It is possible that some of the beneficial effect from these diets may be due to lower dietary intake of vitamin D; the actual amount of vitamin D in commercial diets is difficult to know for certain as this is not a required label disclosure. Some cats that show an initial decrease in serum calcium concentration following any type of dietary change will have a return to hypercalcemia over time.

Q: Are alkalinizing diets (or at least less acidifying diets, like renal diets) effective in the treatment of IHC?
A: The feeding of veterinary renal diets may result in normocalcemia in some cats with IHC though this is less studied than changes to a higher fiber diet. However, in one study, 2 of 15 cats with CKD developed ionized hypercalcemia after being fed a low phosphorus and protein diet. Ionized calcium normalized after discontinuing dietary phosphorus and protein restriction in these instances (Barber 1999) – see below for more about renal diets and hypercalcemia. Renal diets are generally low in calcium and phosphorus and are considered alkalinizing or at least less acidifying than maintenance diets. Chronic dietary acidification increases the availability of the ionized form of calcium in the intestinal lumen facilitating absorption. This also can increase bone resorption as a buffering response to chronic acidosis which contributes to an increase in circulating ionized calcium in normal cats (Ching 1989) and so could potentially contribute to hypercalcemia in disease.

Q: I have heard that a dietary change to one restricted in calcium content restores normocalcemia in some cats with IHC. Do you agree, and which diet would you recommend if so?
A: This is true anecdotally. Some cats return to normocalcemia when calcium content is restricted to < 2.0 G per 1000 calories in the diet. This response could be due to the restricted calcium intake alone, but it could also occur from changes in vitamin A and vitamin D content that are occurring at the same time. There is no overall “winner” for the diet to be chosen. It is also important to remember that the nutrients used to make commercial pet food change frequently so the calcium content in any given diet can sometimes be different every 6 months.

Q: Is it true that some CKD cats develop hypercalcemia when fed renal diets with a high degree of phosphorus restriction (high Ca:P ratio)?
A: YES this appears to be true in some CKD cats, especially those with early IRIS stage CKD. The feeding of a moderately restricted phosphate renal diet restored normocalcemia based on ionized calcium concentration in most of the cats that developed hypercalcemia during the feeding of a more restricted phosphate renal diet. A likely mechanism contributing to the development of hypercalcemia in CKD cats during dietary phosphate restriction is from the increased bioavailability of calcium for intestinal absorption that develops as a consequence of a higher Ca:P ratio (Tang 2021, Geddes 2021, Schauf 2021). The role, if any, for lower phosphorus in the diet to increase the renal synthesis of 1,25D that could contribute to increased circulating calcium has not been reported.

GLUCOCORTICOSTEROIDS
Q: I have read that glucocorticoids work in IHC - do you think I should go ahead and give them? I am frightened of the side effects that could happen after I start them.
A: Cats are more resistant to the side-effects of glucocorticosteroid administration than are dogs and require higher doses to become immunosuppressed. This treatment historically has been the second choice after dietary change failed to restore normocalcemia, but we now consider this AFTER bisphosphonate treatment has been given. If an insufficient response to bisphosphonates is seen, glucocorticosteroids are prescribed in addition to the bisphosphonate. Glucocorticosteroids decrease serum calcium by decreasing intestinal absorption of calcium, decreasing renal tubular calcium reabsorption, and decreasing skeletal mobilization of calcium. There may be a salutary effect from this treatment that changes intestinal calcium absorption in cats with underlying IBD be reducing inflammatory infiltrates. We recommend starting prednisolone at a dose of 5-10 mg/cat/day, rechecking in 4 weeks, and dose escalating by 5 mg every month as needed up to 20 mg/cat/day. It is important to not prescribe glucocorticosteriods before the diagnosis of the hypercalcemia has been established with some certainty, otherwise cytolytic effects in LSA and myeloproliferative disorders will make definitive diagnosis difficult or impossible. A mild calcium-lowering effect can be exerted by use of glucocortocosteroids in other forms of MAH and in those with primary hyperparathyroidism. It is also preferred to have biopsy-proven IBD before the start of glucocorticosteroids. Glucocorticosteroids can be very effective in restoring normocalcemia in many cats with IHC, though higher doses may be needed and some cats escape the initial beneficial effects with a return to hypercalcemia.

Q: Is it OK for me to prescribe prednisone to cats with IHC, or should I consider prednisolone?
A: Oral prednisolone is superior to oral prednisone in cats. This may be due to less GI absorption of prednisone or decreased hepatic conversion of prednisone to prednisolone in cats (Graham-Mize 2005). Long-term glucocorticoid administration to cats can result in development of diabetes mellitus and contribute to muscle wasting that is already problematic in some cats with ICH. Polyuria and polydipsia are less common side-effects than that encountered in dogs treated with glucocorticosteroids.

BISPHOSPHONATES
Q: I hear that oral bisphosphonates can be dangerous in people at times. What kind of side-effects COULD occur in cats and what have you actually encountered?
A 1: Hypocalcemia is the most commonly reported serum biochemical abnormality following bisphosphonate therapy in humans, though hypophosphatemia and hypomagnesemia also can occur. Mild hypocalcemia is sometimes encountered during oral alendronate treatment of IHC in cats (Hardy 2008), but overt clinical signs are not usually encountered. One cat with IHC that was treated with IV pamidronate developed moderate and then severe ionized hypocalcemia 5 and 6 days respectively after treatment; this cat also developed severe hypophosphatemia (Whitney 2011).
A 2: Drug-induced esophageal damage (esophagitis and esophageal stricture) and gastritis are of concern in humans taking oral bisphosphonates. Studies in dogs suggest a direct adverse effect of alendronate on the esophageal mucosa rather than a simple mechanical effect from the pill. The presence of alendronate in the esophagus of dogs for 1 hour only caused minor mucosal damage. However, esophagitis is exacerbated if gastric juice containing alendronate is refluxed into the esophagus. It is thought that alendronate sodium is converted to free acid in the presence of gastric juice (Peter 2002). No esophageal lesions and trivial gastric lesions (deemed not clinically significant by the pathologist) were reported from necropsy in cats undergoing relatively high doses (3 mg/kg once weekly for 22 weeks followed by 9 mg/kg twice a week in tuna juice for 27 weeks) of oral alendronate for 49 weeks (Mohn 2009).
A 3: Osteonecrosis of the jaw (ONJ) occurs rarely in humans receiving bisphosphonates, usually in those with IV dosing and poor oral hygiene. ONJ has recently been described in cats treated to date with oral alendronate. Experimental Beagle dogs receiving alendronate for years have been reported to develop microscopic lesions of ONJ but without macroscopically visible oral lesions.

Q: Is there a role for IV bisphosphonates (pamidronate, zoledronate) in the treatment of IHC?
A: IV treatment with bisphosphonates is almost never needed in IHC since the hypercalcemia is chronic and the cats are usually not in an acute crisis. In the cat with hypercalcemic crisis (encephalopathy, weakness) one dose of IV bisphosphonate can be given while awaiting the oral bisphosphonate to become effective. On occasion, doses are given IV when clients cannot medicate their cat. Also, an IV dose is sometimes given in order to see the effect on circulating calcium when oral bisphosphonate administration has not been effective.

Q: Is oral alendronate safe and effective in restoring normocalcemia in cats with IHC?
A: YES, most cats respond with a return to normocalcemia during dose titration of alendronate. YES oral alenronate appears to be safe in the short term. Oral bisphosphonate (alendronate) treatment is usually recommended when dietary modification has been unsuccessful in restoration of normocalcemia. Unfortunately, once weekly oral alendronate is sometimes chosen by clinicians before an adequate dietary treatment challenge has been employed. The safety and efficacy of oral alendronate treatment for 6 months in 12 cats with IHC has been reported (Hardy 2008). In this study, alendronate was effective in lowering ionized calcium in all the cats after dose adjustments and no side effects were noted other than hypocalcemia in a few instances. There were no side effects noted in a single cat treated with oral alendronate for 18 months which successfully maintained normocalcemia at an average dose of 10 mg per week (Whitney 2011). Recent reports have shown adverse bone effects in some cats on long term oral alenronate treatment (see later).

Q: What would be your typical treatment protocol when prescribing oral alendronate to treat IHC in cats?
A: We typically start at 10 mg once a week. Given the risk of esophagitis and stricture associated with oral bisphosphonate treatment in humans, extra caution is advised to prevent esophageal tissue damage following oral alendonate administration. We recommend “buttering” the cat’s lips/nose as this has been shown to increase salivation and swallowing which contributes to decreased transit time and less time for mucosal contact from the pill (Griffin 2003). Five to 6 ml of tap water is administered via syringe to provide an additional measure to prevent the pills from getting caught in the esophagus (Westfall 2001). Using these preventative measures, we have not observed any signs of esophagitis in cats treated with alendronate thus far. Any food in the stomach can drastically reduce the absorpiton of alendronate to near zero – bisphosphonates are poorly absorbed at best. The oral bioavailability of alendronate administered in water to cats was recently reported to be about 3.0%. This figure reduced by approximately ten-fold when alendronate was formulated in tuna juice (Mohn 2009). To maximize intestinal absorption of alendronate, we recommend an overnight fast for 12 hours prior to the adminstration of medication, give the pills in nothing else besides tap water, and then feed the cat two hours later. Ideally, an 18-hour fast prior and 4-hour fast post-pill is recommended to achive oral bioavailability of 3%(Mohn 2009). We do not recommend any kind of alendronate that has been formulated by compounding pharmacies in flavored solution or suspension due to the likely severe decreases in intestinal absorption***.***

Q: How do you adjust the dose of oral alendronate?
A: We reevaluate the cat’s ionized calcium level 2-3 weeks after starting the 10 mg weekly dose of alendronate. If the ionized calcium has declined substantially but is not yet in the normal range, we recommend waiting another 3 to 4 weeks to see if a further reduction in circulating ionized calcium will occur. Some cats return to normocalcemia on 10 mg oral alendronate per week, whereas others require a higher dose to do so. If the ionized calcium remains above the reference range at this next visit, increase the dose to 20 mg once each week. If the ionized calcium is increased only slightly above the reference range, alternate giving 10 mg one week followed by 20 mg the next (average of 15 mg per week). We do not advise splitting the 10 mg alendronate tablet as this may increase the chances for toxic injury to the esophagus. Once the ionized calcium enters the reference range, we recommend reevaluation in 1, 3, and 4 to 6 months if the ionized calcium is stable and within the reference range.

Q: How long can oral alendronate be safely given to cats with IHC?
A: We do not know. We have quite a few cats that have been on oral alendronate for several years without known toxic effects. Humans taking bisphosphonates are limited to 3 to 5 years of treatment – bone health can diminish in humans after a certain tipping point of bisphosphonate accumulation in this tissue. Reports of adverse effects on bone during long term treatment with alendonrate have recently emerged in cats (see drug holiday later).

Q: A colleague of mine mentioned that chronic treatment with bisphsophonates can lead to bone toxicity in cats. Is this true?
A: Yes, in cats that have been treated with oral alendronate for a long time, usually years. Osteonecrosis of the jaw (ONJ) and pathological fracture of the patellas have been reported. We have also observed fractures of the proximal tibia in a series of cats on long term alenronate treatment (unpublished).

Q: Are there any indicators that bones are at risk for fracture in cats receiving long term oral alendronate?
A: Yes. One such indicator is an increase in the thickness of the tibial cortex. This is more readily identified when baseline radiographs are available to compare changes in bone thickness over time.

Q: Are there any indicators for increased risk that osteonecrosis of the jaw (ONJ) will develop during longterm oral alendronate treatment?
A: Yes. Poor oral hygiene and dental health prior to or during chronic treatment with oral bisphosphonates are risk factors for ONJ to develop during these treatments. It is recommended to provide great dental care before starting this type of treatment. Draining tracts and exposed bone below the gingiva along with oral pain are compatible with ONJ. The bisphosphonate should be discontinued, but any immediate beneficial effect is unlikely due to the very long half life of bisphosphonates that persit in the bones.

Q: I have heard about the use of a “drug holiday” for some treatment protocols. Is a drug holiday appropriate to consider in my IHC cats on longterm treatment with alendronate?
A: YES in those that have maintained normocalcemia for 6 months or longer. Normocalcemia has been maintained in some IHC cats for a long time after stopping alendronate treatment (unpublished case series Dr. Louise Murray). The effect is likely due to the very long half-life of bisphosphonate in bone.

Differential Diagnosis of Hypercalcemia: HARDIONS+G Acronym
H*:* Hyperparathyroidism (1°, 3°, hyperplasia), HHM, houseplants, hyperthyroid

A*:* Addison's disease, aluminum toxicity, vitamin A, milk-alkali

R*:* Renal disease, raisins (grapes)-dogs, renal diet (cats)

D*:* Vitamin D metabolite toxicosis; drugs, calcipotriene (Dovonex), dehydration, DMSO (calcinosis cutis), diet

I: Idiopathic (cats), infectious, inflammatory, immobilization

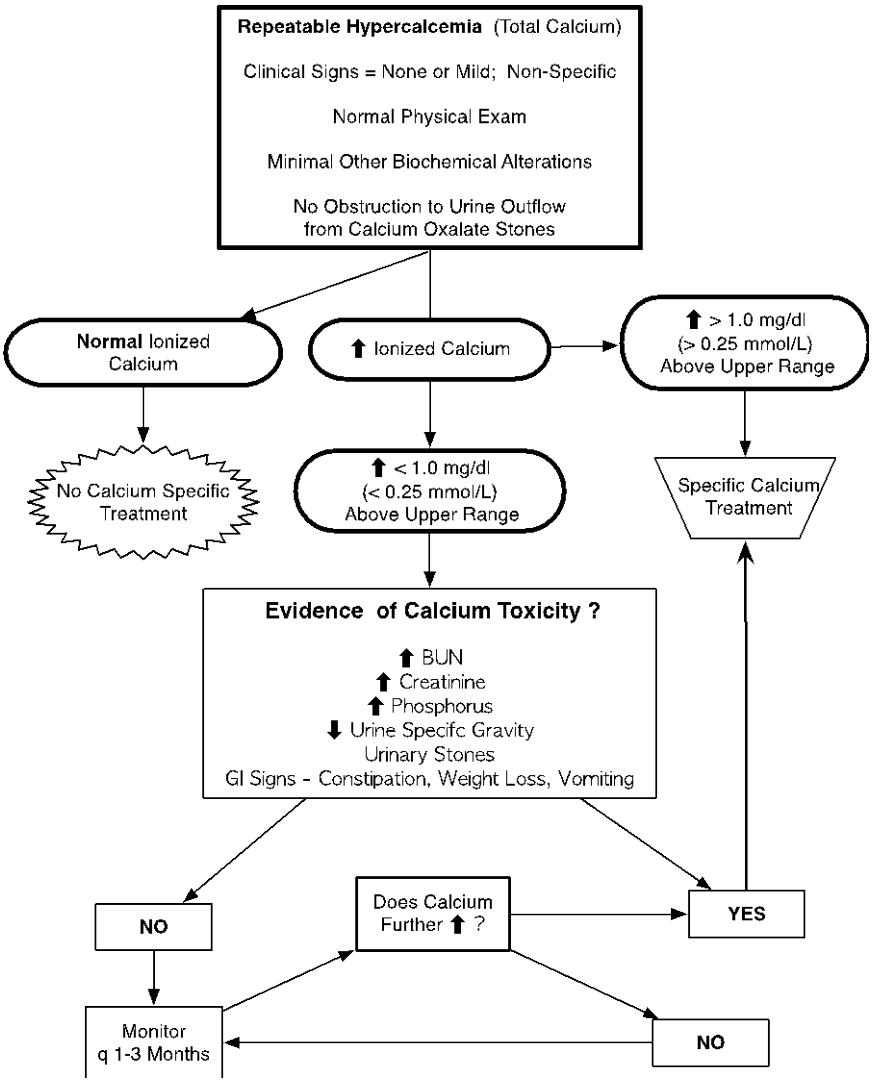
O*:* Osteolytic (osteomyelitis, immobilization, local osteolytic hypercalcemia, bone infarct)

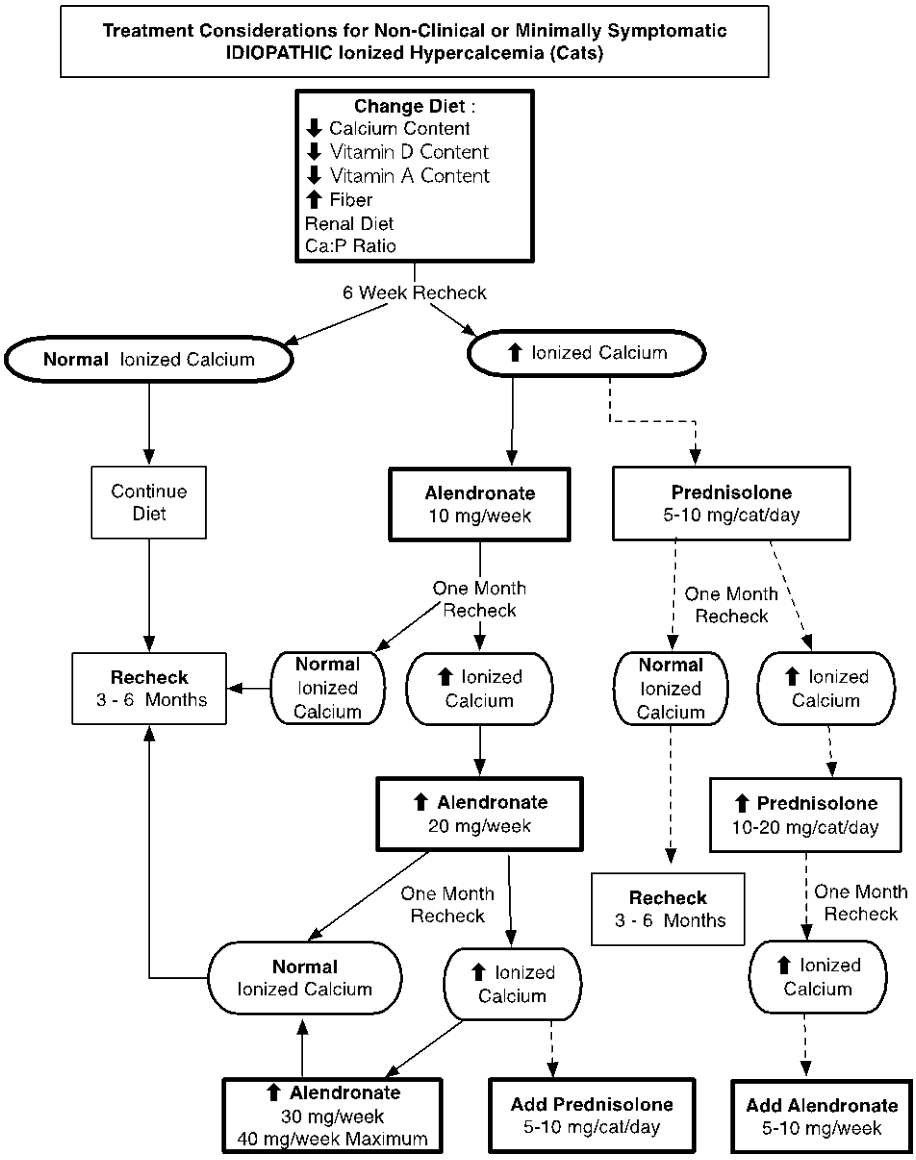
N*:* Neoplasia (HHM and LOH), nutritional

S*:* Spurious, schistosomiasis, salts of calcium, supplements
+
G*:* Granulomatous diseases (fungal)

DMSO, Dimethylsulfoxide; *HHM,* humoral hypercalcemia of malignancy; *LOH, local osteolytic hypercalcemia.*

Chronic Hypercalcemia - Not Sick
Intent to Treat or Not ?





"Pearls" from Dr. Dennis Chew – Idiopathic Hypercalcemia (IHC)

1. Ionized calcium is the biologically active fraction within total calcium.
2. True hypercalcemia based on ionized calcium is detected far less commonly when only increases in total calcium are evaluated in cats.
3. "Corrected" total calcium formulas are not recommended as they often provide misleading information.
4. Prediction of ionized calcium using various formulas is not recommended in general unless there is no possibility of actually measuring ionized calcium.
5. Direct measurement of ionized calcium is the gold standard for evaluation of calcium disorders.
6. Clinical signs in cats with IHC are often subtle, and frequently missed by cat owners and their veterinarians (mild weight loss, occasional vomiting).
7. With undiagnosed hypercalcemia in a relatively well cat < 10 years of age, the odds are high the underlying cause will be IHC. Primary hyperparathyroidism should still be ruled-out.
8. Slight weight loss or decreased lean muscle mass are early clinical signs in some IHC cats.
9. With undiagnosed hypercalcemia in a sick cat, the odds for malignancy are high especially that associated with LSA or squamous cell carcinoma (SCC). One must also rule out hypervitaminosis D and other systemic processes capable of creating hypercalcemia.
10. Acute rescue treatment protocols to lower the magnitude of hypercalcemia associated with IHC are almost NEVER needed.
11. The most consistently effective treatment for IHC to date has been once weekly PO administration of alendronate. This may be less true in the future as we continue to learn how to implement dietary change more effectively.

12. Special caution must be taken to ensure that the alendronate tablets do not stick in the esophagus (oral water and “buttering” of the lips) to avoid esophagitis and possibly gastritis.
13. The average cat with IHC responds to 10 mg PO weekly alendronate, though we do have some cats that require 30 mg/cat/week. We usually do not exceed 40 mg/cat/week.
14. Osteonecrosis of the jaw (ONJ) can develop in some cats on long term oral alendronate.
15. Pathological fractures of the patella and tibia occur in some cats on long term oral alendronate.
16. A “drug holiday” should be prescribed for cats that have been on oral alendronate that have returned to a state of normocalcemia for over 6 months.
16. The cause of IHC in cats remains a mystery, but it is likely that something about the diet creates and maintains the hypercalcemia in many of these cats.
17. It is difficult to determine the amount of dietary calcium, vitamin D, and vitamin A on a per 100 kcal intake basis, as this is not provided on the food label. It requires calling the company or looking this up in diet formulation booklets provided by some of the food companies.
18. Some IHC cats return to normocalcemia when a diet restricted in calcium intake is prescribed. This level of calcium is typically below 2.0 G per 1000 calories of intake, though in some cases < 0.6 G per 1000 calories may be needed.
19. Feeding a diet with a Ca:P <1.4 in addition to calcium content restriction on an energy basis results in the restoration of normocalcemia in some cats with IHC (yet to be published).
20. As we get better with dietary modification, drugs may no longer be needed to manage IHC in cats.
21. Dietary change (using the concepts mentioned above) should be implemented as the first line of treatment In IHC cats that are stable and with minimal clinical signs.

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NOTES:

Should You Extract This Tooth? Using Diagnostics to Decide (Probing, Intraoral Radiography, & CBCT)

Jan Bellows, DVM, DAVDC, DABVP

Choosing between extraction, crown amputation with gingival closure or following a cat with dental disease can be challenging. Approximately 60% of cat teeth are located subgingivally. Fortunately, there are diagnostics available to help decide when to extract.

Probing
The Williams periodontal probe with millimeter markings at 1,2,3,5,7,8,9,10 works well to evaluate the cat's gingival sulcus or pocket. The clinical or probing depth is the distance between the base of the pocket and the gingival margin.

Inserting the periodontal probe into the gingival sulcus or pocket and recording millimeter findings is called probing. With gentle pressure the probe will stop where the gingiva attaches to the tooth. Every professional oral hygiene procedure conducted under general anesthesia should include probing and charting. Cats normally have probing depths less than 1 mm. A periodontal pocket is a pathologically deepened gingival sulcus. The clinical (absolute) pocket depth is the distance from the gingival margin to the base of a pocket, measured in millimeters.

Gingival recession results in the exposure of the root surface by apical migration of the gingival margin. Periodontal attachment level (PAL) is the measurement of periodontal destruction in cases of gingival recession where little or no pocketing exists. The PAL is measured from the base of the gingival sulcus/periodontal pocket to the cementoenamel junction. The clinical pocket depth plus recession (measured from the cementoenamel junction to the gingival margin) equals the total periodontal attachment loss.

Two methods of probing are spot and circumferential. Spot probing is the insertion and withdrawal of the probe at a single area per tooth. Because single areas do not represent the entire tooth, an inaccurate assessment may be obtained. Circumferential probing is insertion of the probe into the sulcus or pocket in at least four places (two buccal and two lingual/palatal) around the tooth, recording millimeter readings. This method compensates for inaccurate readings when subgingival calculus or isolated areas of vertical bone loss are present.

The furcation is a normal anatomical area at the trunk of a multi-rooted tooth where the roots begin to diverge. Normally, this area is sealed from the oral environment by the periodontium. When the integrity of the periodontium has been lost at the furcation, involvement or exposure occurs. Intraoral radiographs are helpful in locating furcation involvement. Radiolucency in the furcation suggests furcation exposure. There are three recognized stage of furcation disease:

- F 1 involvement is diagnosed when an explorer can just detect an entrance to the furcation. A portion of alveolar bone and periodontal ligament is intact at the furcation. Generally, there will be less than 1 mm exposure
- F 2 involvement occurs when an explorer can enter the furcation but does not exit the other side. The undermined furcation is occluded by gingiva or bone on one side.
- F 3 exposure is diagnosed when the periodontium is destroyed to such a degree that the furcation is open and exposed. An explorer can easily pass from side to side.

Criteria for extraction based on probing-
It depends on the tooth- without radiographs, estimate the length in millimeters. If the probe extends greater than half the length of the root then the tooth needs to be extracted. Also, if there is significant mobility in any direction or up and down, the tooth needs to be removed. With radiographs the measurement of loss of greater than half support is easier to measure.

Intraoral Radiology

Periodontal Disease
Radiography of the lamina dura of each tooth should be inspected to see whether it is continuous or interrupted. A complete lamina dura generally indicates good periodontal health. In cases of early and established periodontal disease, the coronal lamina dura appears radiographically indistinct, irregular, and fuzzy. Resorption of the alveolar bone with advanced stages of periodontal disease leads to widening of the periodontal ligament space and loss of lamina dura. When viewing the lamina dura and the periodontal ligament space, only the interproximal portions are

visible. The buccal and lingual walls of the alveolus do not project a lamina dura since they are perpendicular to the x-ray beam. The periodontal ligament space normally appears radiographically as a uniform radiolucent area between the lamina dura and tooth root. It is normally wider in younger cats and narrows with advancing age.

Periodontal disease can be classified from Stages 1 to 4 based on severity of radiographic and clinical signs. The radiograph is used indirectly to determine degree of bone loss. The bone height in periodontal disease decreases as inflammation increases and bone is resorbed. 40% of the bone's thickness must be destroyed before it is detected radiographically. Distribution of bone loss is classified as either localized or generalized, depending on the number of areas affected. Specific areas of bone loss may be classified as horizontal (perpendicular to the tooth) or vertical (angular along the side of the root).

- Stage 1 - gingivitis, occurs when the gingiva appears inflamed. There is no periodontal support loss or radiographic change.
- Stage 2 - early periodontitis, occurs when attachment loss is less than 25%, as measured from the cementoenamel junction to the apex. Clinically, early periodontitis is typified by pocket formation or gingival recession. Radiographically, stage 2 disease appears as blunting (rounding) of the alveolar margin in addition to bone loss. There may also appear to be a loss of continuity of the lamina dura at the level of the alveolar margin.
- Stage 3 - moderate periodontitis, is diagnosed when 25-50% of attachment loss occurs. The direction of bone loss may be horizontal or vertical (angular)**.**
- Stage 4 - advanced periodontal disease, is typified by deep pockets and/or marked gingival recession, tooth mobility, gingival bleeding, and purulent discharge. Attachment loss is greater than 50% of the root length.

Alveolar bone expansion clinically appears as bulging alveoli around one or both maxillary and/or mandibular canines. Radiographically, this lesion appears as bone loss around the root and expansile alveolar bone growth. Tooth extrusion (also called supereruption) occurs when one or more of the intact canine teeth appear longer than normal. Radiographically, the affected teeth have marked loss of periodontal support. Hypercementosis appears as excessive deposition of cementum, usually at the apical third of the root in response to chronic inflammation or abnormal occlusal forces. Ankylosis is the union of cementum with the alveolar bone through destruction of the periodontal ligament

Fractured Teeth
Radiography is essential for evaluation of a tooth affected by endodontic disease. Radiographic images of the teeth and tissues around the root help to define the extent of endodontic disease and prognosis for the tooth. Pulp tissues appear radiolucent. The radiograph of an endodontically affected tooth is examined for the following:

- apical closure, which is necessary for conventional endodontic therapy
- tooth fracture
- abnormalities in the root canal, such as obstruction or resorption
- periapical pathology, such as widened periodontal ligament space at the tooth's apex secondary to bone resorption.

All (even the slightest) fractured teeth in cats should be followed radiographically. Due to the thin covering enamel, treatment (endodontics or extractions) treatment is indicated especially if the cat is young. Periapical lucency indicates the presence of disease within the bone around the teeth.

Periapical disease is a pathologic process surrounding the apex of one or more roots that is due to either inflammation or necrosis of the dental pulp from trauma, infection or occurs as an extension of periodontal disease. The radiographic appearance of periapical disease consistent with a granulomatous lesion (periapical granuloma) is widening of the apical periodontal ligament space with circumscribed alveolar bone resorption. A homogeneous radiolucency at the apex or a dark halo in the periapical tissues is typical of an abscess. A sharply outlined circumscribed radiolucent area is commonly caused by a periapical cyst, which usually arises from a preexisting granuloma.

Criteria for extraction of fractured teeth. If the pulp is exposed or nearly exposed in a young or mid-aged cat either root canal therapy or extraction is indicated. If the cat is older and there is no pulp exposure the cat can be clinically and radiographically followed.
Criteria for crown reduction (amputation, coronoectomy,) followed by gingival closure. Indicated in type 2 tooth resorptions where gingivostomatitis is not also present.

Tooth Resorption
External root resorption may also result from periapical inflammation, orthodontic therapy, or from unknown stimuli. Radiographically, external resorption appears as radiolucent defects on any area of the root surface. Internal resorption arises from the pulp. The cause is unknown, but trauma or pulpitis from anachoresis (bacteria gaining access to the injured pulp through vascular channels) are believed to be contributing factors. It can be difficult to determine whether a lesion is due to internal or external resorption. If a normal-appearing root canal is visualized radiographically, the lesion is considered external in origin.

Tooth resorption is classified as:

- Stage 1 (TR1) - mild dental hard tissue loss (cementum or cementum and enamel).
- Stage 2 (TR2) - moderate dental hard tissue loss (cementum or cementum and enamel with loss of dentin that does not extend to the pulp cavity)
- Stage 3 (TR3) - deep dental hard tissue loss (cementum or cementum and enamel with loss of dentin that extends to the pulp cavity); most of the tooth retains its integrity. Internal resorption radiographically appears as focal enlargement of the root canal
- Stage 4 (TR4) - extensive dental hard tissue loss (cementum or cementum and enamel with loss of dentin that extends to the pulp cavity); most of the tooth has lost its integrity
- Stage 5 (TR5) - remnants of dental hard tissue are visible only as irregular radiopacities, and gingival covering is complete

In addition to the above classifications, some investigators believe that three radiographic appearances of tooth resorption should be distinguished in order to create a treatment plan based on clinical and radiographic findings:

- type 1 - a focal or multifocal radiolucency is present in the tooth with otherwise normal radiopacity and normal periodontal ligament space
- type 2 - there is narrowing or disappearance of the periodontal ligament space in at least some areas and decreased radiopacity of part of the tooth
- type 3 - features of both type 1 and type 2 are present in the same tooth. A tooth with this appearance has areas of normal, narrow or lost periodontal ligament space and there is focal or multifocal radiolucency in the tooth and decreased radiopacity in other areas of the tooth

Criteria for extraction of teeth affected by tooth resorption – Extraction is indicted when either the tooth resorption has extended to the oral cavity evidenced visually or through probing with an explorer, or there is marked loss of dental hard tissue located subgingivally.

CBCT-Cone Beam CT
Compared to intraoral DR and CR, CBCT is a more specific and sensitive diagnostic tool for evaluation of individual teeth, bone invasion and extension of oral tumors into the nasal cavity, caudal pharynx, and orbit as well as dental trauma. It is also ideally suited for evaluating the TMJ pathology. The CT image data are reconstructed slice by slice in the transverse plane, using a filtered back projection for each slice. The entire mouth and adjacent areas can be scanned within one minute. General anesthesia is necessary.

In a 2019 published study comparing 32 cats with created dental lesions, CBCT led to significantly higher confirmation than that of dental radiography for 4 of 14 categories (missing teeth, horizontal bone loss, loss of tooth integrity, feline resorptive lesions), and higher, although not significantly so, for 9 categories (supernumerary teeth, supernumerary roots, abnormally shaped roots, vertical bone loss, buccal bone expansion, periapical disease, inflammatory root resorption, and external replacement root resorption). In conclusion, we found that CBCT provided more clinically relevant detailed information as compared to dental radiography. Therefore, CBCT should be considered better suited for use in diagnosing dentoalveolar lesions in cats.

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NOTES:

Role of Dietary Phosphorus in Feline Renal Health & in Management of CKD

Stacie Summers, DVM, PhD, DACVIM (SAIM)

Introduction

Chronic kidney disease (CKD) is common in cats, especially in senior cats. CKD is an umbrella term to describe any renal disease that leads to progressive loss of function over time. There are many documented causes of CKD, such as infection and upper urinary tract obstruction, but many times the underlying etiology cannot be identified in cats at the time of diagnosis. Although dietary phosphorus is an essential nutrient in cats, recently high dietary phosphorus intake, particularly inorganic phosphorus, has been linked to kidney injury in cats. While healthy cats require dietary phosphorus, intake is generally restricted in those cats with phosphorus retention and CKD.

Phosphorus Regulation in Pet Foods

The Association of American Feed Control Officials (AAFCO) and the European Pet Food Industry Federation (FEDIAF) provide nutrient concentration guidance for commercial pet foods.[1,2] Manufacturers that sell pet food in the United States are required to include nutritional adequacy statements on labels. The FEDIAF is a trade association that provides guidelines that its members and other manufacturers in Europe follow with self-regulation. Both AAFCO and FEDIAF base their nutrient guidelines at least partly on the data summarized by the National Research Council (NRC), which provides dietary requirements for cats.[3] These published guidelines from AAFCO, FEDIAF, and NRC are established based on interpretation of the published literature and expert opinion. Currently, AAFCO states a minimum phosphorus concentration in commercial cat foods (1.25 g/1,000 kcal), and NRC reports a minimum phosphorus requirement for cats (0.35 g/1,000 kcal). There are currently no safety limits or dietary maximums for dietary phosphorus cited in globally accepted feline nutrition guidelines.[1-3] However, some food manufacturers have internal standards for their products.

Dietary Phosphorus Sources and Effect on the Kidney in Health

Phosphorus is an essential nutrient in cat food and is absorbed in the small intestine. Intestinal absorption of phosphorus is affected by the total amount of phosphorus, the sources of phosphorus in the diet, and the relative amount of calcium to phosphorus in the diet (Ca:P ratio). Phosphorus in commercial cat food is supplied from either organic or inorganic sources. A low Ca:P ratio (high phosphorus compared to calcium) increases phosphorus absorption in the intestines. Organic phosphorus is sourced from raw materials used for manufacturing of pet foods, including animal tissue and grains. Inorganic phosphorus sources are added to the diet and listed on the food label (e.g., phosphoric acid).[4] Inorganic phosphorus is better absorbed and is more bioavailable than organic phosphorus.[5]

Acute and chronic phosphate nephropathy is well documented in people and leads to acute tubular injury and tubular atrophy, interstitial fibrosis, and interstitial inflammation. In healthy young adult cats, experimental diets with inorganic phosphorus concentration greater than 3.6 g/1000 kcal and low Ca:P ratio (<1) decreased glomerular filtration rate, induced changes in renal echogenicity, increased renolith formation, and glucosuria in some cats.[6,7]
Over-the-counter cat foods labeled for healthy adult and senior cats were found to have highly variable amounts of total dietary phosphorus owing to the lack of a published phosphorus maximum in commercial cat foods. Approximately 30% of adult and senior diets had a high total dietary phosphorus concentration (>3.6 g/1,000 kcal) and few had a low Ca:P ratio (<1).[8,9] As such, care should be taken when choosing a long-term diet for cats, especially those with a predisposition to CKD (i.e., senior cats). Avoiding diets with high inorganic phosphorus and low Ca:P ratio (<1.1) in cats is encouraged to avoid potential kidney injury and hormonal disturbances in calcium homeostasis.[10,11]

Dietary Management of CKD in Cats

The objectives of nutritional management in cats with CKD are to (1) slow progression of disease, (2) provide sufficient energy to maintain body weight, (3) alleviate clinical signs of uremia, and (4) manage fluid, electrolyte, and acid-base disturbances. The goals of nutritional management vary between individual cats and stage of disease. In general, therapeutic renal diets are restricted in phosphorus and high-quality protein, of which some diets are below the AAFCO minimum for adult maintenance. Therapeutic renal diets tend to have a high caloric density, be low in sodium, and be alkalinizing. The amount of potassium in these diets is highly variable. There are several studies that proven the benefit of feeding a renal therapeutic diet to cats, and International Renal Interest Society (IRIS) suggests that a renal diet be considered in cats with stage 2 disease and recommends a renal diet for cats with stage 3 and 4 disease. Clinical studies have shown that renal diets lower plasma phosphate, incidence of uremic crisis and renal-related death as well as prolong survival.[12-15] Recent studies have shown that feeding a phosphorus-restricted diet in cats with early-stage kidney disease can cause hypercalcemia in some cats, and increasing phosphate intake may

lead to normalization of serum calcium.[16,17] However, further research is needed to elucidate which cats with CKD are at risk of hypercalcemia.

When feeding a therapeutic renal diet to a cat with CKD, maintaining normal caloric intake is of upmost importance to prevent protein malnutrition. To determine the number of calories a CKD cat should eat per day, you first calculate the resting energy requirement (RER) based on body weight and then multiply the RER by a factor of 1.0-1.4 (based on body condition score) to obtain a maintenance energy requirement (MER).

If patient is < 2.0 kg: RER = 70 * (Body Weight in kg)$^{0.75}$

If patient is > 2.0 kg: RER = (30 * Body Weight in kg) + 70

MER for CKD cat: RER x 1.0-1.4

If a cat refuses the therapeutic renal diet, consider the following options:

1. Treat nausea and dysrexia. Several comorbidities in cats with CKD, such as anemia, dehydration, metabolic acidosis, and hypokalemia, can cause dysrexia. These comorbidities, if present, should be addressed and in doing so may improve the cat's appetite. You can also consider treating the symptoms with drug therapy. Maropitant (Cerenia®) is an oral tablet that has been shown to palliate vomiting associated with CKD, however, did not improve appetite or body weight.[18] Transdermal mirtazapine (Mirataz®; 2 mg every 48 hours) was shown to increase appetite and resulted in weight gain in cats with CKD.[19] Capromorelin oral liquid (Elura®) for cats is a ghrelin receptor agonist that can be used in CKD cats to stimulate appetite.
2. Gradual transition to the new therapeutic renal diet over 4-8 weeks. This may be achieved by mixing the old and the new food together while gradually decreasing the amount of the old food and increasing the amount of the new therapeutic renal diet.
3. Rotational feeding. Cats with CKD are known to be picky eaters. Offering different varieties (brands, flavors, textures, etc) of therapeutic renal diets may entice the cat to eat more.
4. Entice the cat to eat. Try warming canned food or offer frequent, small meals. Place dish in stress-free and easily accessible area where the cat spends most of its time. Supplement the diet with a low-sodium chicken broth or tuna juice in moderation. If there is competition for food in the household, consider a cat feeder with a collar sensor.
5. Esophagostomy tube. If all the above does not get the cat to be fully transitioned to a therapeutic renal diet, you may consider recommending an esophagostomy tube. An esophagostomy tube is a valuable tool in the maintenance of nutrition and hydration in some cats with CKD. Many medications can be administered through the feeding tube which improves compliance.
6. Supplementing a therapeutic renal diet with an over-the-counter diet. Some owners of CKD cats with dysrexia may choose to supplement or feed exclusively an over-the-counter diet to their cat. Historically, senior cat foods were recommended as an alternative to a therapeutic renal diet, however recently it has been found that the nutritional content of senior foods is highly variable.[9,20] This is likely attributable to the lack of established nutritional guidelines for senior cats. If necessary, an over-the-counter food that has a phosphorus content <1.6 g/1,000 kcal and protein content <100 g/1,000 kcal should be fed as an alternative to a therapeutic renal diet. Only a minority of senior cat foods fit these criteria. Veterinarians should avoid broad recommendations regarding commercially available senior cat foods, and in general choose a reputable science-based brand with a veterinary nutritionist on staff.

How to Compare Nutrient Content Between Foods

To comply with federal and state regulations, pet food manufacturers must provide a guaranteed analysis on the food label. At minimum, the guaranteed analysis must provide the percent by weight of crude protein, crude fat, crude fiber, and moisture. When comparing the nutritional content of pet foods, veterinarians and pet owners cannot use the guaranteed analysis, because the ingredient amounts are only listed as maximum or minimum (not an absolute amount) and the 'as fed' basis does not take into account the moisture and caloric density of the food. To compare diets, we need to convert the average or typical analysis (percent 'as fed' basis) to energy basis (for example, g/1000 kcal). To do so, you need two pieces of information: the average or typical analysis from the company in a percent 'as fed' basis and the caloric density in kcal/kg. See below for an example.

For a dry cat food with a minimum protein of 35% (as fed) and a calorie density of 4,000 kcal/kg, what is the protein level on an energy basis?

1000 * (protein % ÷ kcal/kg) = g/100 kcal

1000 * (35/4,000) = 8.75 g/100 kcal

Some companies may also provide the nutritional content in energy basis in published food guides.

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NOTES:

2022 Spring into Feline Medicine

THREE-DAY **VIRTUAL LIVE CE EVENT**

Sunday, April 24th | Wednesday, May 4th | Saturday, May 14th

ALL TIMES ARE EASTERN TIME ZONE

Sunday, April 24, 2022

TIME	SESSION TITLE	SPEAKER	SPONSOR
12:00 - 1:00 pm	Diagnostic & Therapeutic Approach to Feline URI	Dr. Mike Lappin	Boehringer Ingelheim
1:20 - 2:40 pm	Purrfecting Strategy & CommuniCATion in the FURst Kitten Visit	Dr. Natalie Marks	zoetis
3:00 - 4:20 pm	Feline Fracas: Why Cats Fight & How to Help Them	Dr. Theresa DePorter	
4:30 - 5:30 pm	Easy as One, Two, Pee: Steps for Solving Feline House-Soiling	Dr. Julia Albright	Purina Pro Plan Veterinary Diets

Wednesday, May 4, 2022

TIME	SESSION TITLE	SPEAKER	SPONSOR
2:00 - 3:00 pm	Diagnosis & Treatment of Proteinuria in Cats	Dr. Stacie Summers	Royal Canin
3:15 - 4:15 pm	Ionized Calcium in Cats: How Much are You Missing Without This Measurement?	Dr. Dennis Chew	zoetis
4:45 - 5:45 pm	Should You Extract This Tooth? Using Diagnostics to Decide (Probing, Intraoral Radiography, & CBCT)	Dr. Jan Bellows	Dechra
6:00 - 7:00 pm	Role of Dietary Phosphorus in Feline Renal Health & in Management of CKD	Dr. Stacie Summers	Royal Canin

Saturday, May 14, 2022

TIME	SESSION TITLE	SPEAKER	SPONSOR
12:00 - 1:20 pm	Hospice & Palliative Care: The Foundations for the Role of the GP	Dr. Mary Gardner	Lap of Love Veterinary Hospice & In-Home Euthanasia
1:40 - 2:40 pm	The Old Cat in the Clinic: How Senior Wellness Visits Improved Charlie's Quality of Life	Dr. Myles McKenna	zoetis
2:50 - 3:50 pm	The Itchy Cat	Dr. Mike Rossi	Ceva
4:00 - 5:00 pm	Frustrating Felines: Inappetant Cats	Dr. Diane Delmain	Purina Pro Plan Veterinary Diets

Hospice & Palliative Care: The Foundations for the Role of the GP

Mary Gardner, DVM

Almost every time the door opens, I am greeted with a crying client. As a veterinarian that limits my practice to in-home hospice and euthanasia, it is something I encounter daily with my families. In those moments, I give a warm smile, a gentle handshake and in many cases, a big hug.

Although the majority of our appointments are for euthanasia, we also offer veterinary hospice care to our concerned pet parents. However, veterinary hospice is still very misunderstood, even within our profession. I am often asked, "What is veterinary hospice?" at clinics and conferences. It is important to first understand what hospice is NOT: It is not prolonging suffering nor is it euthanasia or natural dying. Hospice simply is a medically supervised service dedicated to providing comfort and quality of life for the pet (and the owners) until euthanasia is elected or natural death occurs.

A great deal of families wish to keep their pet alive for as long as possible while also maintaining a good quality of life but simply don't know how and feel helpless. As a veterinary hospice practitioner, I am able and willing to help extend life as long as pain and anxiety are controlled, but this is always preceded by a lengthy discussion on the progression of the disease process present and a clear "stop point" which we agree is the ending of a good quality of life. Communication, preparation, and more communication is the hallmark of a successful hospice case.

At Lap of Love, many of our clients are referred to us from veterinary specialists – mostly oncologists, cardiologists and internists. While much of veterinary hospice is ideally done in the home, where the pet is most comfortable, many discussions and treatments should be started at the clinic with their primary veterinarian who has enjoyed a long-term relationship with the pet parent. With that being said, I am sad to report that approximately 40% of our clients have not taken their pet into the clinic within the last 2 years. I strongly believe that we can help a great number of pets if we are able to educate owners on the aging process and also the progression of the specific diseases their pets are facing.

Veterinary medicine focuses a lot on 'Senior Wellness' but I think we are asleep at the wheel when it comes to geriatric pet care. Caring for a geriatric pet is a completely different experience than caring for the 8 yr old 'senior dog'. Care giving for the elder pet can be emotionally and physically exhausting and it is vital to support the owners through this time. Our philosophy of the way we care for these pets, in most cases, needs to shift from curing but to simply caring. This quote from Jurassic Park is a favorite of mine, "Just because we can, doesn't mean we should". Too often owners tell me that they are scared to continue with their regular veterinarian because they are simply forced into xrays or bloodwork. Often hospice is simply a tool to help the owners grasp the idea that their pet's life will be ending soon. It may be a month or even just a day – at this point radiographs are pointless – but pain medication, education, communication and preparation is priceless.

Although providing hospice in the home can garner a lot of information that may be missed at the clinic, the discussion and treatment can start with you. Setting up a hospice program in your clinic is actually very simple.

It is most important to help the family understand the disease process their pet is facing. Although we cannot predict exactly what will happened in the future, we can use our medical training and experience to give each family facing an end-of-life experience with their pet a possible and probable progression of their pet's disease process. As doctors, this is the most important piece of information we have to give them and the most valuable tool families have in the decision-making process. We must, to the best of our ability, explain the most likely "natural" method of death if left unattended. This educated approach to the physicality of death is essential to veterinary hospice care; by providing the family with knowledge and expectations, we give them the ability to make an informed decision based on their personal wishes for their pet with the gentle guidance of their veterinarian.

I break down the hospice consultation and care into 5 pillars. Medicine, Environmental Management, Caregiver Concerns, Quality of Life Discussions and Euthanasia Conversation.

1. Medicine – There is nothing mysterious about hospice care – when I was in general practice, I was caring for advanced aged pets or those with terminal illness – but I never actually called it hospice. At this point in time, it comes down to Palliative Care – keeping them comfortable. The vast majority of my cat and dog patients have some form of pain – typically arthritis. Managing pain is paramount to keeping them comfortable. Next would be to control any mental changes – namely cognitive dysfunction. But anxiety, aggression and other

changes can occur as a pet ages. Nausea is seen often in organ failure and cancer patients. Lastly, inappetence also becomes a concern with some diseases and there are now much better appetite stimulants available. Inappetence is a huge factor to pet owners in determining quality of life.

2. Environmental Management – I am lucky to have the ability to enter families homes to see how the environment is for all residents. Tile and hardwood floors are in almost every home I visit and simply placing bath mats or yoga mats around the house will help those weak and wobbly pets. I teach owners about keeping them safe and blocking off areas of concern like steps, dark areas, pools, etc. There are other wonderful products available to help pets with certain ailments – like harnesses, toe grips, halos (for vision), night lights, etc.

3. Caregiver Concerns - Not until I dealt with the struggles of caring for my own geriatric pet, did I fully appreciate what caregiver burden was really all about. You love your pet, you will do what you need to do – but it's hard physically and emotionally.

   With our pets we also have the burden of deciding to euthanize when appropriate. And that in itself is a heart wrenching decision. Quality of life is a very subjective thing and pet owners may not always know when it's time. Pet owners do know their pets best but they still may need guidance. And they may end up with guilt if they feel they've waited too long. It's the one conversation that we have the most with families seeking end of life services.

   A cross sectional observational study was done by Spitznagel, Jacobson, Cox, Carlson entitled "Caregiver burden in owners of a sick companion animal: a cross-sectional observational study." This was the first study that examines the toll of caregiving on pet owners. It measured the mental health of owners by monitoring levels of depression, stress and anxiety as well as Quality of Life enjoyment for the owner. (Comparable measurements have been studied in human caregiving relationships to assess similarities)

   The results showed that caregivers of terminally or chronically ill pets had:
   - Greater level of caregiver burden and stress
   - Greater perceived stress
   - Greater symptoms of depression and anxiety
   - Lower on indicators of quality of life and enjoyment

   Providing support and guidance is massively important for the family as they go through the intense management and emotional struggle of caring for a hospice patient.

4. Quality of Life Discussions - How I wish the answer to the question 'when is time' was simple and clear cut – however, it is not. It is our duty to assist owners with end-of-life decisions and to help end and prevent suffering of animals. There are many ways to help families explore quality of life questions but the one way that is an injustice to our profession is if you simply say, 'Call me when it's time'. Owners need more than this and animals deserve more. There is a great deal of information on our website for owners faced with this decision.

5. Euthanasia Conversation – I always have a brief conversation about what the family's wishes are for the passing of their pet. Although no one wants to be the one to actually make the decision, often times the passing of a pet is done via euthanasia. I want the family to understand the process but also discuss as a family unit how they would like the event to go. Who will be present, what the pet may eat before/during, what memorial items they may want to keep, etc. It helps them plan for the best experience possible. It also sets expectations for what services you provide (how far in advance do they need to know, do you go to the home, etc).

By using the word 'Hospice' with your clients, it redirects their thoughts from curing their pet to caring for their pet and preparing themselves for death and grieving. Then, you can tailor your medical management appropriately to make sure the pet is kept comfortable and safe.

Hospice care is not a mystery and something all clinics should offer. The AVMA advices clinics that if they do not provide hospice, they should refer to someone who does – but I don't see any reason for that. The hardest part is the conversation and often we are very busy at primary care clinics. But this type of service will bond families to you more than ever!

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The Old Cat in the Clinic: How Senior Wellness Visits Improved Charlie's Quality of Life

Myles McKenna, MVB, MVetSci, MVetMed, DACVIM (SAIM), DECVIM-CA, MRCVS

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The Itchy Cat

Michael Rossi, DVM, MNS, DACVD

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Frustrating Felines: Inappetant Cats

Diane Delmain, DVM, DABVP (Feline)

Inappetence is a common and frustrating issue in feline medicine. It is important to understand drivers of appetite in healthy cats and external factors that influence food intake. There are many helpful medical options for treatment, as well.

Maintaining food intake is especially vital in cats as they have a propensity towards developing potentially fatal hepatic lipidosis with decreased intake. Cats have a high protein requirement and will catabolize muscle if food intake is insufficient. Finally, appetite is strongly linked to quality of life. It is important to calculate energy needs and monitor intake and weight in sick cats.

Hyporexia is defined as a decrease in appetite and inability to need metabolic needs. This session will cover treatment options for the hyporexic cat. Anorexia is the complete lack of appetite and food intake. If anorexia occurs for more than 3-5 days in a cat, a feeding tube must be placed to meet energy and protein needs.
Many factors are involved in driving appetite in cats: social/environmental, food and physiological ones. Cats are unique carnivores, evolving from a desert cat that lived and hunted alone. Domestic cats maintain many of their ancestor's characteristics. Free-roaming cats will hunt multiple small meals of low caloric density, high protein prey items daily. Cats are both a predator and prey species, making them very alert and wary of environmental changes. Domestication helped cats learn the advantages of group living and they will form social groups that share resources. These groups recognize each other and their territory by sharing a common scent. However, the group will not care for or feed sick individuals.

Social and environmental factors may influence appetite. Some cats prefer privacy, while other will eat more with company or petting. Cats prefer a routine and consistency of care. Competition with other pets should be prevented. A clean, quiet, safe environment with familiar scents should be provided.

Many food factors are involved in appetite. Cats have a small number of taste buds, detecting mostly amino acids and acidic tastes and can actually taste water. Olfaction and "mouth feel" are also used to sense food. Cats use their taste buds, entire mouth and olfaction to determine whether they will eat a particular item. In general, they prefer foods that resemble fresh prey: high protein, moist, body temperature and a high-water content. Cats dislike items that resemble carrion: cold and bitter tasting items are particularly off-putting. Cats are extremely individual in their preferences and these should be known for each cat. Offering a variety of different foods, textures and cooked meats may be helpful. Soft foods should be warmed, especially for older cats. Flavor enhancers such as probiotics, food supplement pastes, chicken broth or even a dash of garlic powder may stimulate some cats to eat. It is important to avoid food aversions when treating sick cats, as these may last for life. Food aversion may be associated with pain or unpleasant experiences, nausea or oral force feeding.

Hydration must be maintained, as dehydrated cats are reluctant to eat. Cats have a low thirst drive and are inefficient drinkers, so dehydration is common in many conditions. Hydration options include IV or SQ fluid administration or an oral osmolytle supplement.

There are many medical options for appetite enhancement, but these should not replace diagnosis or treatment of underlying problems. Medical appetite enhancement is particularly helpful in the diagnostic phase of illness, palliative care and to maintain muscle mass and quality of life in chronic illnesses. Options include: Cobalamin, anti-nausea medications and appetite enhancers. Cobalamin is involved in many metabolic processes. Deficiencies are common in many chronic and GI diseases, resulting in anorexia, GI signs and in severe cases, neuropathies. Supplementation often results in improved appetite and energy levels. The injectable form is dosed weekly, while the oral form requires daily administration. Rarely, hypersensitivity may occur. Nausea and vomiting must also be controlled. Maropitant, a central anti-emetic neurokinin receptor agonist and Substance P inhibitor, is widely used in cats. The injectable form is labeled for use IV or SQ in cats, with a wide safety margin. Refrigeration may reduce SQ injection site pain.

Mirtazipine, a tetracyclic antidepressant, stimulates appetite in cats by blocking serotonin receptors which function on pathways that lead to appetite inhibition. It also enhances norepinephrine, which acts on appetite stimulation pathways. Mirtazipine also has anti-nausea effects. A transdermal product is labelled for cats to be applied to the pinna daily. Mirtazipine tablets are extra-label but have been used in cats for many years. The most common side effects include agitation, vomiting, vocalization, ataxia, tremors and hypersalivation. Caution should be used in cats

with liver disease. There is an increased risk of serotonin syndrome if used in conjunction with other drugs that affect serotonin. Increased sedation may occur if administered with benzodiazepines.

Cyproheptidine, a serotonin agonist and an anti-histamine, is also an effective appetite stimulant in cats. It is extra-label, but supported by long term usage. Cyproheptidine may be administered up to every 12 hours. The tablets are small and often easy to administer, but the taste is difficult to hide in compounded liquids. Common side effects include vocalization, mild sedation or agitation. It should not be used in patients with severe renal or liver disease or hyperthyroidism. Cyproheptidine has a strong affinity for serotonin receptors and may be used to reverse mirtazapine toxicity. It should not be used in conjunction with tricylic anti-depressants, SSRI's, tramadol or CNS depressants.

Capromorelin is a ghrelin receptor agonist and stimulates appetite through the release of growth hormone. It was recently approved for cats with CKD and resulted in weight gain in a study. It is generally well-tolerated and dosed daily. Reported side effects include emesis, hypersalivation, lip smacking, head shaking, inappetence, behavior changes and lethargy. Due to growth hormone release, capromorelin should not be used in cats with acromegaly and may increase glucose levels in diabetics. It should be used with caution in cats with heart disease or severe hepatic or renal issues.

Diazepam may be considered in some feline patients. It blocks GABA receptors, thereby blocking pathways that inhibit appetite. IV injection results in mild sedation, ataxia and immediate food ingestion. Paradoxical excitement sometimes occurs, and patients are very sensitive to noise. Oral usage is contraindicated, as it may result in fatal hepatic necrosis.

Gabapentin has recently been shown to stimulate appetite in healthy young cats, but more research is needed. Gabapentin has analgesic and anti-convulsant effects and its mechanism is not fully understood. It is widely used in feline practice to decrease anxiety associated with veterinary visits.

Cannaboids are an area of interest for appetite enhancement but there is only limited information in cats. Limited studies of human labeled products have been performed in dogs. While these products were widely used in veterinary medicine almost a century ago, current regulation of these products falls into a grey zone of state, federal and FDA regulations. Many OTC cannaboids are marketed to veterinarians and animal owners as supplements despite a lack of oversight. The AVMA cautions veterinarians on their usage.

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NOTES:

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