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Expert views from a roundtable on inappetence



ABBREVIATIONS

CKD Chronic kidney disease

Managing Inappetence & Chronic Kidney Disease

Inappetence is a concern frequently encountered in veterinary practice. In cats, chronic kidney disease (CKD) is a common cause of appetite changes. CKD patients are often presented with some level of inappetence, whether it is anorexia (complete lack of appetite), hyporexia (decreased appetite), or dysrexia (change in eating pattern or behavior). Reframing the way we think about inappetence can lead to improved outcomes in these pets. Knowing which tools are available to address these feeding concerns, as well as having strategies to leverage owner involvement, can be the keys to success in this patient population.

Dr. Wood: How do you feel about the word “inappetence,” and how would you define it?

Dr. Bullen: I personally use it interchangeably with anorexia, but I will qualify the description as well because a lot of our patients come in with progressive dysrexia to hyporexia to anorexia. So, I might say, “Molly presented for inappetence,” meaning anorexia, then I qualify by asking how long it has been going on and the severity.

Dr. Larsen: Some other ways we describe dysrexia in the context of a

specific patient would be that they have a selective appetite, then qualify that like they’re willing to take treats or eat human food, but they won’t eat a CKD or hydrolyzed diet.

Dr. Wood: What is cachexia and sarcopenia? What are the differences between those?

Dr. Bullen: When I think of cachexia, I think of the loss of lean muscle mass associated with an active disease state. So, it tends to be more of an active process. Typically, it’s associated with increased inflammatory cytokine circulation. Oftentimes, it’s

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—Dr. Bullen

associated with an increased energy need, depending on what it is, but you get this increase in lean muscle mass breakdown, whereas sarcopenia tends to be loss of lean muscle mass associated with age, and that sometimes can be due to an increase in inflammatory mediators, but a lot of times, it's inactivity. You can have both; you can have a cachectic process and also age-related sarcopenia. Sarcopenia is not ideal, but cachexia is more alarming and more important to really try to get a handle on, if one can. It's very challenging to support the patient appropriately.

Dr. Larsen: Dr. Bullen, do you think that the distribution of muscle loss in a particular patient helps determine the underlying cause?

Dr. Bullen: I personally do. When I think of some age-related changes, especially if it's associated with inactivity or disuse or things like that, it tends to be the muscle that they should be using to ambulate and mobilize. When I see muscle loss associated with cachexia, it tends to be the muscles you wouldn't necessarily see associated with disuse—the temporalis muscles, the epaxial muscles, things like that. So, when I'm assessing a patient for muscle mass scoring or muscle mass indexing, I'm looking at everything but also assigning localization. I'll say moderate muscle wasting, generalized, and if it's truly generalized, that worries me if it's all over. If I see moderate muscle wasting for a limb and normal muscle

mass everywhere else, we really need to be isolating that limb, seeing if it is disuse, if there's an injury, that sort of thing. So, yes; localization and distribution can help me determine if it's more likely to be sarcopenia versus a cachectic process. By the time they get to me, I usually know that they have a chronic disease state in which cachexia is more common or likely, so it's already on my radar.

Dr. Larsen: For certain patients, I'm often looking more at the musculature on their head, those temporalis muscles and such, because we see so many geriatric patients that have some degree of degenerative joint disease, so maybe their pelvic limbs are atrophied and sometimes they're not symmetrical because we know they have an injury on a side. Then sometimes the patient's conformation or maybe their underlying orthopedic disease makes the epaxial muscles really difficult to determine, if the spine is just prominent, or if the muscle is atrophied or both, due to ankylosing spondylosis. Sometimes it's even harder when they have a layer of adipose on top of those muscles and you can't palpate easily, especially in that location. Most of our patients are geriatric and have multiple comorbidities.

Dr. Marks: I think one misconception among GPs is sarcopenia is sort of normal—that it's just age, they're going to waste, and that's just what happens. But I think that it's really important for us to stress that both of these things mean something and

we should identify and look into it. With sarcopenic patients—and I'm thinking of the older geriatric cat that has sarcopenic change down the lumbar spine—remember almost 80% of older cats have lumbar arthritis. A lot of that change is easily reflected on a visual exam. These findings should trigger investigation of some kind, whether it's pain control, diagnostic imaging, nutritional support, or a combination. I think it is our responsibility, especially with today's pet parent, to offer possible treatment plans and solutions. I treat cachexia clinically; it's a little more worrisome because that typically means I'm looking for cancer or something else that's quite inflammatory or metabolically challenging, but I still look at my sarcopenic patients and think there must be something else—an injury, a cruciate, or something that's triggered these changes that I still want to investigate. It just may not be with the emergent nature sometimes of the cachectic patient.

Dr. Wood: Aside from potential underlying conditions, why do we want to avoid cachexia in these patients? Why is cachexia itself also a problem we want to address?

Dr. Marks: From a practical standpoint, my cachectic patients are on a downward spiral. They're burning energy that they typically don't have reserves for. They're breaking down important parts of their body that they are not going to replace. Their organs are not in the best state with

regard to their energy supply, so they're starting to deteriorate. So, when I see a cachectic patient, I am really on a hunt to find the reason for the cachexia. I'm also concurrently trying to figure out how I can best support this patient so this spiral doesn't continue. And you're typically fighting these 2 battles at the same time—because, if you don't identify the underlying process quickly and get a handle on it, they're burning the candle at both ends.

Dr. Bullen: A lot of the processes that result in cachexia are the same processes that result in dysrexia, hyporexia, and anorexia. So, with the addition of cachexia, which typically increases metabolic needs, tissue stores start breaking down. Then, on top of that, you might have some form of dysrexia, anorexia, or hyporexia, so now we are leading to this protein energy malnutrition; we're in a complicated state of starvation, not a simple state. It is a lot harder to come back from that. When you don't have stores to begin with, time is very limited to try to treat the disease process. If I can at least make them stop continuing to waste away from their depleted stores, that'll make my ability to treat their disease a lot better. Having the proinflammatory state and these increased metabolic needs makes my job medically and nutritionally a lot harder and makes them less responsive to some treatments. So, if I can stop that, I might be able to prolong their lifespan and quality of life, and they might be more responsive to some of the things I'm doing.

Dr. Wood: Can we see cachexia in our feline patients, even if they appear to be eating okay to some degree?

Dr. Larsen: Absolutely. I think that individual energy needs are really challenging to predict. Without quantitative information about the current intake and how that compares with past intakes, you can

absolutely have an owner who thinks their cat is eating great. And it's not just that the owner's being a poor historian. Cats can be secretive about their illnesses and their food intake behavior. They tend to be fed ad lib more than dogs, so you can have very overt evidence of malnutrition and the clinical history you get from the client doesn't correlate with that necessarily.

Dr. Bullen: It could be harder in a multi-cat household as well. So not only are they often fed ad lib, but you have another cat that's eating all the food, and they just keep filling the bowl up.

Dr. Wood: What are some other reasons we can see cats with CKD having decreased appetite?

Dr. Marks: I think a big reason in general practice is the inability to understand how to transition foods. It's very common for a GP to diagnose CKD. The first thing we want to do is put them on a prescription diet. But, we know that, if transitions for cats are abrupt, it can cause them to be incredibly food adverse. We can see them go from a cat that might be hyporectic to one that's completely anorexic and refuses to even go back to their original food. We're always acting with the best intentions, but sometimes we can be too impatient or have an improper introduction to prescription diets that can really add to that wasting disease.

Dr. Larsen: It's also the nature of cats to have really fixed flavor and texture preferences. And cats with CKD don't just have azotemia; they often have acidosis, they're anemic, they're dehydrated, maybe they have a secondary UTI or ureteral obstruction. They probably have a lot of reasons why they don't feel well and don't want to eat adequate amounts of food. And one thing I tell clients is that people who are on dialysis or have uremia from kidney disease say that food doesn't taste or smell the way that it used to. And medications can do that, too. So we're adding reasons on top of all these underlying conditions that really negatively impact food intake.

Dr. Bullen: A lot of the CKD population tends to be middle-aged to geriatric. As we age, the smell and taste receptors can start to decline, so you have all of these reasons to not be interested in food. I always emphasize to my clients that most cats need anywhere from 10 to 14 days to transition to a new diet, but when I have a sick cat, I'm saying it may take 14 to 21 days to transition to the new diet, and they might even need longer. It's just always trying to emphasize that every pet is truly unique in their flavor and form preferences, even in their transition tolerance, and to really just try to be patient because it's an investment in the long run. If they can get them onto a product that is nutritionally beneficial, it can absolutely extend their quantity and quality of life,

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but we have to be patient. There's only one appetite hormone, but there are a lot of reasons for them to be anorexic, dysrexic, or hyporexic and to not have a good appetite.

Dr. Wood: Regarding improving the appetites of these cats with CKD, are you using appetite stimulants in these cats? Are you using them long-term? Short-term?

Dr. Larsen: At our institution, we're fairly aggressive with feeding tube placement. A lot of our cases get esophagostomy tubes, most frequently when we're talking about cats. Of course, you're going to have patients or clients for which that's not an option for a variety of reasons. Mirtazapine and capromorelin are the appetite stimulants that I think people reach for first in terms of the likelihood that they'll work the best. We have other ones that people talk about sometimes, but we don't see the benefits. One thing that we're always cautioning people about when they're reaching for appetite stimulants is you still need to track intake and make sure that you're still meeting your goals and that you are not thinking that you're just fixing it by sending home an appetite stimulant, because we want to make sure that the owner's able to administer it and that it's having the effect we actually want it to have.

Dr. Wood: What would be the effect we want it to have? How would we say to owners this is what we want you to look for?

Dr. Larsen: I'm a big fan of owners having kitchen gram scales for food and baby scales for the cat. Unless we're doing an exclusively canned diet and it happens to be a nice fraction of a can, we are giving gram amounts for our feeding instructions, so we have initial targets for calorie intake based on an equation, then we monitor and adjust from there. We don't know if that's actually going to be adequate to either maintain body condition score (BCS) and muscle condition score (MCS) or improve it, depending on what our goals are. So assessment and readjustment is really important to serial nutritional assessments.

Dr. Bullen: I think one of the things that is really helpful in that regard is taking a little bit of ownership. Our clients are busy. They love their pet, but if we can help them with that process and send home tracking charts, a calendar, reminders, or things to make it easier for them to actually document the goal, that can be very helpful. I keep track for every single patient. Everybody has their own spreadsheet, and it has the starting calories, starting weight, and weigh-ins. So, I just put it in the sheet when they come in or when we email and get a response. Don't get me wrong—I don't have the time to call them 5 times if they haven't responded to me, but at least I have reached out to them to remind them, and that can be very helpful for the client to visually see that maybe their cat isn't eating enough—especially if they're in that limbo phase of

not needing a feeding tube yet. I'm with Dr. Larsen. I am super aggressive with feeding tubes. If they presented for anorexia, it's already too long. We need to be having that discussion. Oftentimes, when I diagnose a new CKD case, there's a little blurb somewhere down below about assisted feeding, and I talk to the clients and say we're not necessarily ready for this yet, but I like to have the conversation early so they're not surprised when it's an emergency. I always give them the opportunity to eat voluntarily but absolutely use the feeding tube if they can't or if they choose not to. I love feeding tubes because I give enteral water and I don't have to poke them with SC fluids all the time. I also use capromorelin and mirtazapine. I love that there is a masking agent in Elura® (capromorelin oral solution). But there are definitely things that we can do to help our clients document how their pet is doing so we can give them guidelines for next steps. And a lot of time, that's just what they need: a little bit of quantification because it's hard to just eyeball it, especially if there're other cats or animals in the house.

Dr. Marks: I think client communication is one important point to take out of this. I think the other is, in general, many small animal veterinarians feel uncomfortable placing tubes, even though it's an easier procedure than we think after you've done a few of them. But because of our own potential inexperience placing them, I think that unfortunately

spills over into our lack of recommending them. We need more education about assisted feeding and the concurrent use of proactive appetite stimulants, not reactive appetite stimulants. Early intervention and proactive use is when we're most successful; that's the case with most diseases, but especially with this, when we wait too long and wait until they're really far down that road, no matter what we do, the prognosis is not as good. This is a great time for the entire veterinary team to get involved with these clients and these families, because it's difficult for one veterinarian to do at a practice with every other thing they have going on. We really need a team approach.

Dr. Wood: When do you start recommending appetite stimulants in those cases when the patient doesn't need a feeding tube just yet or the owners have decided not to do a feeding tube? Which one might you choose first and why?

Dr. Marks: I've become much more clinically aggressive as I've learned more about inappetence and the prognostic indicators that are better for longer term success for kidney patients. If there's any form of inappetence, just a couple of days of dysrexia or a pattern of hyporexia, I add it in the first time I have that information from the client. I think that also has triggered me to be incredibly proactive with the client services team in how they triage these patients when clients call. We used to do a lot of phone fixes many years ago when we didn't know any better, but we know now that appetite changes mean something.

Dr. Bullen: I would agree with that as well. I am in a slightly different situation; a lot of clients are coming to me directly because their pets aren't eating. I would say most cases that come to me have some form of hyporexia or dysrexia. With every one of my cases, if there is any dis-

cussion about hyporexia, dysrexia, whatever, they get a full page that is filled with toppers, and the toppers are actually calculated out for that individual patient. We do 5% of their total caloric intake if they are getting treats and 10% if they're not getting treats. Then we also put in recommendations for heating the food, changing the bowls, cleaning the bowls, and then at the bottom, there is always a recommendation for appetite stimulants with the dose. And when we send that treatment plan, they also get a prescription. They have everything they need so, if the steps that we have discussed don't work, they have those appetite stimulants in their arsenal and they're ready to go. If they see me in person, they will leave with an appetite stimulant. They don't have to use it, but they're leaving with it. There's also guidelines on when I recommend instituting it. If they come in already anorexic or with a prolonged history of dysrexia or hyporexia, you should go ahead and start that, because what we're dealing with now is not normal. If the pet is intermittently finicky in terms of appetite but their weight, BCS, and MCS are stable, then I say, "Okay, here are parameters for when to start the appetite stimulant. I typically use transdermal mirtazapine or capromorelin/Elura. What I choose is truly dependent on the individual. If my client has trouble with oral medications, I will recommend Elura second and transdermal mirtazapine

first because I don't want to negatively impact the bond with their parent. If they think that they can give it and they have no problem, historically, I will often recommend Elura first. It honestly depends on what they've tried historically, what the relationship is like, and what the individual patient is like as well.

Dr. Wood: Do you have endpoints? What are those endpoints?

Dr. Bullen: I personally use capromorelin long-term. I personally feel comfortable using it, especially if it's end of life. With those expectations, we have the conversation with clients about intermittent use. We know the normal negative feedback loop is intact with daily use, but it may not be with intermittent use. And there's enough within the safety studies that I feel relatively comfortable doing it. Very rarely do I dose reduce. I have on occasion, but those I usually reserve for severely cachectic, muscle-wasted, poor body conditioned patients, but oftentimes I don't.

Dr. Marks: It does feel better, of course, to have the FDA approval for long-term use in CKD cats. For a lot of veterinarians, the FDA approval is a huge factor. It feels better, especially with cats, where we have to use so much extra-label. It feels good to have those studies to show that we do have the safety to use long-term, and it doesn't have to be this

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short honeymoon phase where the cat feels better, then all of a sudden you have to take it away.

Dr. Larsen: One thing I think deserves a little more attention is some owners are working really hard and putting a lot of effort into achieving adequate intake, so the pet is doing well and their weight's stable, but that kind of effort is just not sustainable. I think that alone can be an indication for intervention, and I think it's something that we often don't recognize as readily. Those care-taking tasks are really demanding and underappreciated, even by the person that's doing them, because they're in the grind, and they can't even look up and realize how much it's impacting their life, because maybe it happened gradually. They care so much, and they really want to help and be a part of the healthcare team; it is our job to make that as easy as we can and to provide some of those more practical solutions that might help them, whether that's simplifying a home-cooked diet or the medication schedule so that they're not having to do something every hour.

Dr. Wood: For cats with CKD, we know they are going to be on other medications as well. How often are you recommending monitoring for these patients? What other things should we be thinking about regarding how we're monitoring them?

Dr. Marks: From the clinical GP side,

I think there's actually quite a bit. For me, it's not just SC fluids and canned food, because I think that we often get into this rut of, "Oh, another kidney cat. I'm just going to send home a bag of fluids and canned food, and we'll see them back in three months and see how things go." There's just so much more to dive into between the physical exam and the clinical pathology, the blood pressure measurements, and any other diagnostic imaging that we're doing, the comorbidities that we're managing, taking all of that and looking at the nuanced and subtle changes to make sure we aren't missing anything. We're being very proactive and aggressive in our recommendations and goal setting with the client—within reason, of course, but we're looking at obviously controlling protein, phosphorus, weight, and anemia. We're looking at calorie management, hydration, defecation frequency, comorbidities, and if we're managing hyperthyroidism, then also managing worsening kidneys due to the thyroid disease treatment. There's so many things to consider, and we know now there are so many more screening opportunities with the advent of Renal-Tech, where we can talk to clients at an early stage, and we can actually prognostically sort of look ahead to see what it's in the future in a way to get them prepared even from an earlier age, and talking about SDMA screenings, where we can get a lot more information from the earliest level, whereas before, we had to just wait until we had these elevated cre-

atinines. There's just a laundry list of things that I would love for GPs to understand that your hands aren't tied all the time. And it really needs to be not just internal collaboration but client collaboration, because for us to get reward out of treating these cats, we need a compliant client; otherwise, it can be unrewarding and so heartbreaking to watch these patients do poorly if we don't have a client that's on board with us. I thank my clients. I try to compliment my clients. I constantly check in with them in regard to, "I know we said we were going to do fluids every day. Is that working for you? Or should we think about something else?" Being transparent yourself so that you're approachable and having the whole team on board so that the technicians, the nurses know this is our treatment plan, but this is where we're starting. It doesn't mean this is definitive and etched in stone. This is where we're starting, and it's a breathing, living document, and we're going to change as we go.

Dr. Bullen: I would agree with you as well. There's only so much one person can do. I used to just be by myself, and the services that I wanted to have, I didn't have, and I needed support staff. Now I have amazing nurses that help hold me up; we are able to send automatic recheck emails to ask if they have any questions, if they want to schedule their recheck. All of the plans have monitoring recommendations and guidelines in terms of what I feel is necessary based on the severity of

the disease, based on what other comorbidities they have. Owners are the expert in their pet; it is their job to tell me if our plan is working or not. And if it doesn't work, I welcome them to come and give me that feedback so I can give them plan B. I establish that relationship from the beginning so they feel comfortable coming to me with problems.

Dr. Wood: Let's compare appetite stimulants to some of the other medications cats with CKD are put on, such as maropitant and antacids. How are those different from each other, and what are their roles?

Dr. Marks: From a primary veterinarian perspective, I think a common misconception is the use of maropitant—or really any antiemetic—for concurrent appetite stimulation. We know that's not an indication or necessarily a researched effect of an antiemetic. There are cats that are absolutely going to need both, the cats that have nausea and active vomiting where an antiemetic is absolutely indicated. But I think many clinicians think that just using that one medication is sort of this umbrella for everything else, including appetite stimulation concurrently at the same time. We need to understand that, although antiemetics are indicated in some of our patients, it shouldn't really be the first drug to reach for if the primary goal is appetite stimulation. As patients develop more progressive kidney disease, those uremic toxins wreak havoc on the gastric lining, and that's certainly another reason our patients aren't eating. So, antacid therapy, definitely an indication when used appropriately, but not labeled as an appetite stimulant. So, although all 3 of these medications—appetite stimulants, antacids, and antiemetics—have a place in CKD patients, Elura is specifically designed to stimulate appetite.

Dr. Bullen: One thing I typically will

point out to my clients is that, if there's a lot of underlying causes for anorexia, if we don't get those under control, then the appetite stimulants are less likely to be effective. So, if they think that their pet is nauseous or they have uremic toxins and they need antacids or if they're severely painful and they need analgesics or whatever it might be, then we actually need to have them on both. So we need to take care of the signs making them feel terrible, in addition to ideally managing the disease, then putting them on that appetite stimulant. When I have cases in which the anorexia is refractory to an appetite stimulant, I'll go back and see if we can find other causes we haven't identified and other medications or treatment plans that could help make them feel better.

Dr. Wood: When cats come in with early CKD and maybe their appetites are good and they've only lost a little bit of weight, would you consider intervening with these patients? How proactive would you be?

Dr. Larsen: I think that's an interesting question because we do want to be proactive, but how we actually do that is a whole other question, and that's going to depend on the client and if they're able and willing to provide body weights or more quantitative food intake information to you so you can intervene early. If that is beyond their limits, we need to assess whether they are able to institute

changes, such as being able to provide medication consistently every day for a long period of time. And in some cases, we're managing another disease, and the CKD does not always progress quickly. Until we trend out quantitative food intake and body weight data, I probably wouldn't institute appetite stimulants.

Dr. Marks: We understand there's a gray area, right, and there are nuances to every case and every client, but sometimes it's helpful to have a little bit of guidance of a number, target, or goal just to kind of wrap your head around where you're headed. When I teach about this, the one study I do bring up is the one from the *Journal of Feline Medicine Surgery* that says that >5% weight loss is significant. So, if we're seeing >5% weight loss, I'm concerned, I'm going to intervene. This is when we're going to start something. It helps a client understand that pet's journey and what may be ahead, and it gives them something to track at home as well, and sometimes that helps with compliance.

Dr. Larsen: The other aspect of having a percentage guideline is how fast has that change happened? Was the last weight a year ago or a month ago? If you have serial weights and you've been trending them out while you're suspicious, then you have a much better idea if that 5% has happened over 6 weeks or 6 months. I'm much more concerned if it's happened over a shorter time frame.

They care so much, and they really want to help and be a part of the healthcare team; it is our job to make that as easy as we can and to provide some of those more practical solutions that might help them.

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—Dr. Marks

KEY TAKEAWAYS

- ▶ Inappetence is frequently encountered in veterinary practice and encompasses anorexia (complete lack of appetite), hyporexia (decreased appetite), and dysrexia (change in eating pattern or behavior).
- ▶ CKD is a common cause of appetite changes, and CKD patients are often presented with some level of inappetence.
- ▶ Cachexia and sarcopenia should be identified, differentiated, and addressed.
- ▶ Food transitions should be done carefully in cats, as a leading cause of inappetence is dietary refusal.
- ▶ Feeding tubes and appetite stimulants should be discussed early in the course of disease.
- ▶ Comorbidities should be considered when determining the underlying cause of inappetence.
- ▶ Develop a plan to help owners quantify food intake.
- ▶ Pet owners are critical members of the patient care team, and effective communication is essential.

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Dr. Bullen: Agree. And again, really trying to distinguish with the clients if it's intentional or unintentional. Most of our patients are overweight or obese, so it is entirely possible that you have a fat kidney cat, but maybe the client has actually been calorie restricting, which isn't necessarily desired on certain types of diets, but maybe it was actually one of the goals. I feel like we ask that at least once or twice a week, if pets would actually eat more. When I talk about calorie density, I always have to define what I'm talking about because it's something that they're just not used to thinking about. And if they're switching from one diet to another,

typically but not always, if you go from a maintenance to a renal therapeutic diet, there tends to be more calories packed per cup or per unit in the kidney diet. So we do see a lot of cats potentially blow up if they're in early renal stage. One of the things that we can do is actually calculate out the amount to feed. "Here's what you're currently feeding and the estimated calorie content; here's what we're recommending." So again, clear expectations that we're working together, we'll figure it out, but it does take a little bit of back and forth. It is an iterative process and we have to recheck to make sure we're on the right track.

Indication

Elura is indicated for the management of weight loss in cats with chronic kidney disease.

Important Safety Information

For oral use in cats only. Do not use in cats that have a hypersensitivity to capromorelin, or in cats with hypersomatotropism (acromegaly). Elura may increase serum glucose for several hours after dosing; use in cats with current or historical diabetes mellitus has not been evaluated and may not be appropriate. Use with caution in cats that may have cardiac disease, severe dehydration, or hepatic dysfunction. Elura has not been evaluated in cats younger than 5 months of age, or in breeding, pregnant or lactating cats. The most common adverse reactions included vomiting, hypersalivation, inappetence, behavior change and lethargy. **For complete safety information, please see accompanying product label.**