PURINA Institute

Advancing Science for Pet Health

Purina Institute Handbook of

CANINE AND FELINE CLINICAL NUTRITION

A Reference Guide to Nutritional Management of Clinical Conditions in Dogs and Cats

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INTRODUCTION

The Purina Institute is a global professional organization that serves as the voice of nutrition science. Representing a diverse team of more than 500 scientists and pet care experts across a worldwide network of research and development facilities, the Purina Institute believes science is better when it is shared. That's why we're on a mission to unlock the power of nutrition to help pets live better, longer lives.

Nutrition influences every aspect of a pet's life. As part of the world's largest food and nutrition research organization, the Purina Institute shares Purina's leading-edge research as well as evidence-based information from the wider scientific community with veterinary professionals, aiming to bring nutrition to the forefront of pet health agenda. The Institute does not discuss products, only proven nutritional science.

The last decades have illuminated the important role of nutrition in lowering risk of developing certain health conditions and being an incremental part of disease management. Despite continuous scientific discovery and nutritional innovations, the role of nutrition is often overlooked in clinical practice.

At the Purina Institute, we transform nutrition science into actionable information that you can put into practice to benefit your patients. We partner with hundreds of the world's most respected animal scientists, nutritionists, and thought leaders, pioneering the latest science, and unearthing powerful breakthroughs. Through the Purina Institute's extensive online resources at https://www.purinainstitute.com, publications, and scientific programs, you can stay armed with the unbiased, science-based nutrition information you need to make the confident nutrition recommendations owners want for their pets.

The second edition of the Canine and Feline Clinical Nutrition Handbook is fulfilling the Purina Institute's mission—to empower veterinary professionals, like you, with the latest scientific knowledge, proven nutrition management strategies, and practical algorithms on different health scenarios you can use in your daily practice to further improve and extend the healthy lives of pets through nutrition.

This handbook focuses on therapeutic nutrition for dogs and cats with specific health conditions. Evidence-based tools to help you make every day nutritional recommendations for healthy dogs and cats and for management of disease conditions can be found on CentreSquare™ (https://www.purinainstitute.com/centresquare).

On behalf of the Purina Institute, I would like to thank the scientific editors of the book for putting the scientific content together.

I also would like to thank all the experts who have shared their knowledge and expertise by contributing to the book chapters, resulting in a convenient reference guide for everyday use in veterinary practice.

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PREFACE

There is one thing that is common among all patients seen by every veterinarian—they all must eat! Over the past century, dramatic changes in our understanding about nutrition have helped to greatly reduce or eliminate diseases associated with nutritional deficiencies. Knowledge about essential nutrients and requirements led to the production of better diets that provide complete, balanced nutrition to promote and maintain health. Today, veterinarians have numerous choices of foods they can recommend to their clients with confidence.

Although the vast majority of pets seen by primary care veterinarians are healthy, many eventually develop some health problems that may benefit from a change in diet. These diet-associated conditions may be grouped either as "diet-induced" or "diet-sensitive." A condition that is diet-induced is caused by a problem with the diet or with feeding management. Some examples include developmental orthopedic diseases, caused by vitamin D or phosphorus deficiency or excess calcium or calories; neurological disease in cats caused by thiamine deficiency; or gastrointestinal disease caused by foods contaminated with pathogenic bacteria. Another example of a diet-induced disease could be obesity, as this is primarily due to overfeeding of calories, regardless of diet fed.

A diet-sensitive disease is one where dietary modification can be used to mitigate clinical signs of a disease. Some examples of this include chronic renal disease, which can benefit from restriction of dietary phosphorus or addition of buffering nutrients; sterile struvite urolithiasis in cats that may respond to urine-acidifying diets; or avoidance of specific allergens to reduce stimulation of the immunological cascade in a food-allergic pet. Note that, in these examples, although clinical signs may be addressed, the underlying pathology remains. It also is important to note that diet-sensitive is not the same as diet-induced and changing a diet in an attempt to prevent a diet-sensitive disease is unlikely to be of benefit in healthy pets.

Therapeutic diets are generally designed to address diet-sensitive diseases. Therapeutic nutrition can address the physiological compromises and some of the clinical signs caused by disease but cannot cure the underlying disease.

Many options are available under the umbrella of therapeutic nutrition. In order for veterinarians to provide their patients with the best possible care, it is important to consider the nutritional needs of their patients. This is best addressed by completing a nutritional assessment on each patient. The nutritional assessment includes information such as body weight, body condition score, muscle condition score, and diet history, in addition to medical evaluation. As with the medical history, the nutritional assessment should be updated at each visit to determine any changes made or needed. For patients that would benefit from a therapeutic diet, veterinarians must consider the disease and its impacts, as well as the key nutrients to address those issues. This is especially important with co-morbidities that may have different, or even conflicting, nutritional goals. Finally, it must always be remembered that the first goal of the diet is to provide all the essential nutrients a pet needs, while also addressing the disease-associated modifications.

Compliance with feeding recommendations for pets can be poor, especially in chronic illness. In addition to the objective data gained in the nutritional assessment, it also is important to understand clients' concerns regarding feeding their pets. This may include financial concerns, perceptions about ingredients, a lack of understanding about the benefits a therapeutic diet may provide, or other issues. The more clearly a veterinarian understands his or her client's concerns, the greater the likelihood a recommendation can be made for the patient that will be followed.

Thus, two-way communication—to help you understand your client and to help them understand the value of the recommended diet and feeding management—will provide the best opportunity to address the needs of the patient.

Veterinarians remain the preferred resource for pet owners regarding nutrition and health care advice. Each of the chapters in this handbook is designed to aid veterinarians and their support team to provide patients and their owners with the best nutritional advice, in order to support pets' health and overall quality of life.

Dottie Laflamme, DVM, PhD, Diplomate ACVIM (Nutrition)

EDITORS' NOTE

When we developed and assembled this book, our goal was to create a relevant and easy-to-use nutrition resource for practitioners and veterinary teams. We wanted each chapter to be fairly short, practically focused, and able to stand alone. We hope the book will allow veterinary health care professionals to more easily incorporate nutrition into management of disease conditions and know they are being guided by top global experts.

This book is not meant to be an all-inclusive reference for case management, but instead focuses on clinical nutritional management of common health conditions of dogs and cats. More in-depth information on the topics covered by our authors may be found in the references at the end of each chapter. Information on well-pet nutrition and other topics may also be found at CentreSquare (https://www.purinainstitute.com/centresquare or use the QR code).

Most of the acronyms used in a chapter are defined in the chapter. Acronyms that are used repeatedly may not be defined in all chapters. Key examples are listed below and are defined in further detail in the glossary at the end of the book.

AAFCO – Association of American Feed Control Officials

BCS – body condition score

FEDIAF – Fédération Européenne de l'Industrie des Aliments pour Animaux Familiers or European Pet Food Industry Federation

MCS – muscle condition score

NRC – National Research Council

A big thank you goes to the authors and to everyone who contributed to this project. This book was a large undertaking and was a team effort. We are grateful to everyone for enhancing nutrition education of veterinary health care professionals worldwide and for providing practical nutrition information that can be used to help pets live longer, healthier lives.

Best wishes,

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The opinions expressed in this book are those of the individual authors and do not necessarily reflect the views of Nestlé Purina PetCare or its affiliates

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BRAIN AND BEHAVIORAL DISORDERS

BRAIN DISORDERS IN DOGS AND CATS

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KEY TAKEAWAYS

- Nutrition plays a role in management of brain disorders including cognitive dysfunction syndrome, epilepsy, and paroxysmal dyskinesia.
- The aims of nutritional management are to maintain energy supply for adequate brain function; modulate disease risk factors such as oxygen free radicals, inflammation and altered blood supply; and decrease adverse effects of drugs, as well as improve behavioral comorbidities.

INTRODUCTION

The role of nutrition and its interplay with the gut microbiome and central nervous system (CNS) in health and disease has attracted an increasing amount of attention in recent years. In the past, research focused mainly on describing deficiencies and how they can lead to CNS impairment and accelerate brain aging. In recent years, however, the focus has been on how the addition of specific nutrients, the manipulation of diet, and modifying the gut microbiome can improve CNS function and prevent neural damage. This chapter will discuss dietary management strategies to improve brain health, slow down brain aging, and help nutritionally manage neurologic and cognitive disorders. Because research in cats is lacking, the role of nutrition in brain disorders in dogs will primarily be discussed.

ENERGY METABOLISM IN THE HEALTHY BRAIN[1-6]

Brain tissue requires a large amount of energy in relation to its size, largely for sustaining its activity of adenosine triphosphate (ATP)-dependent sodium potassium pumps, ensuring cell homeostasis of neurons and their membrane potentials, neurotransmitter transporter, and synaptic activity. In a fed state, the brain tissue derives most of its energy from oxygen-dependent metabolism of glucose, which provides a substrate for ATP. The brain is dependent on a constant glucose supply, as it has no glucose storage capacities, and accounts for close to a quarter of the body's glucose consumption.[3,4] Alternative energy sources for the brain are lactate and ketones. Blood lactate levels increase during exercise and can be metabolized by the brain to provide energy; however, the contribution of lactate to the brain's energy needs is negligible. The situation is different for ketones, such as β-hydroxybutyrate and acetoacetate, resulting from metabolism of triglycerides. Ketones can provide up to 60% of the brain energy requirements, especially in times of starvation.[5]

Triglycerides are esters derived from glycerol and three fatty acid (FA) carbon chains. These are defined by their carbon chain length and the degree of hydrogen saturation. Fewer hydrogens mean more double carbon bonds, resulting in either mono- (one double bond) or polyunsaturated fats (PUFAs). Long chain fatty acids (LCFAs) are composed of 16–22 carbons, medium chain fatty acids (MCFAs) of 6–12 carbons, and short chain fatty acids (SCFAs) of less than 6 carbons, respectively. LCFAs are metabolized by β-oxidation to form acetyl-CoA, which is further oxidized by the citric acid (TCA) cycle.

In starvation or diseases causing an alteration of cellular availability of glucose (e.g., diabetes mellitus), oxaloacetate and CoA can be relatively reduced, challenging the TCA cycle. Acetyl-CoA can then be used for the synthesis of ketones, primarily in the liver. In a non-starved state, the diet needs to be low in carbohydrates to stimulate significant ketone production from LCFAs. The challenge for the brain, however, is that it has limited capabilities to store and utilize LCFAs. LCFAs do not easily pass the blood-brain barrier (BBB) and mitochondria of neurons lack enzymatic capacity for β-oxidation. Compared with LCFAs, MCFAs have a higher ketogenic yield, readily pass the BBB, and are oxidized in astrocytes, offering a glucose-sparing effect and serving as an alternative energy source.[1,2] Octanoic acid (8C; caprylic acid)

and decanoic acid (C10; capric acid) are the most important MCFAs for brain metabolism and function. Interestingly, apart from providing an alternative energy source, certain decanoic acids are postulated to have a direct effect on brain function.[2] In low concentration the pro-inflammatory GPR84 receptor can be activated, which can be found on microglia in the brain. The significance of this activation is not clear, as no adverse effects in this regard have been seen in patients receiving medium chain triglycerides (MCTs) chronically. In higher concentrations, capric acid can directly antagonize AMPA type glutamate receptor function, reducing excitatory neurotransmission. Interestingly, this effect has not been associated clinically with a depression of brain function; in fact, patients on MCTs are usually more alert. Furthermore, higher concentrations of capric acid can activate the transcription factor PPARγ2, promoting mitochondrial biogenesis and antioxidant effects, and inhibit mTORC1 (mechanistic target of rapamycin complex 1) signaling pathway, regulating cell proliferation, autophagy, and apoptosis. An activated mTORC1 signaling pathway has been associated with insulin resistance, arthritis, cancer, and other diseases.

ENERGY METABOLISM IN THE AGING BRAIN

The brain's constant high demands on energy for its metabolic processes and function makes it more susceptible to disruptions in energy supply. Aging is associated with a decline in mitochondrial function and glucose metabolism.[3,4] The regional and overall brain glucose consumption is decreased in older dogs by approximately 25%.[3] This can be associated with an increase in oxygen free radicals and can be present prior to measurable cognitive decline.

COGNITIVE DYSFUNCTION – CLINICAL CONSIDERATIONS

The last third of a pet's life is in the senior part of life. With the strengthening of the human–animal bond, more and more owners demand better care for their senior pet. Veterinarians, however, find it easier to recognize orthopedic or chronic medical conditions than cognitive dysfunction syndrome (CDS). CDS is not as readily recognized at first due to its slow onset, often first subclinical and then with initially mild signs, which can only be picked up by standardized and validated questionnaires. Around 30% of dogs aged 11–12 years and 60% of dogs aged 15–16 years show clinical signs of CDS.[7] The most common behavioral change observed in CDS is anxiety, followed by spatial or temporal disorientation, altered interaction with family members and animal companions, changes in sleep–wake cycles, house-soiling, and vocalization (primarily in cats). These changes significantly impact the quality of life for the pet and its caregiver, the owner. In clinical practice, tools such as **DISHAA** (a questionnaire evaluating **D**isorientation, social **I**nteraction, **S**leep–wake cycle, **H**ouse-soiling, learning and memory, **A**ctivity, and **A**nxiety) for dogs and **VISHDAAL** (**V**ocalization, alterations in **I**nteractions [e.g., increased affection], changes in the **S**leep–wake cycle, **H**ouse-soiling, **D**isorientation, alterations in **A**ctivity levels, **A**nxiety, and **L**earning and memory) for cats help owners and veterinarians identify and monitor behavioral signs that may be associated with cognitive impairment and CDS.[1,8]

Clinical signs of CDS can be more severe in animals also affected by dental disease, pain (e.g., from osteoarthritis), systemic illnesses, or other behavioral problems. This should be considered when diagnosing and managing a patient with CDS. The diagnosis can be facilitated by using a standardized questionnaire in senior dogs on a regular—ideally yearly—basis. This will help detect CDS early and help monitor the dog's cognitive decline. Apart from clinical signs of CDS, magnetic resonance imaging of the brain can reveal brain atrophy (widened sulci, ventriculomegaly) and vascular lesions, such as infarcts or microhemorrhages. Recent research into CDS-related biomarkers is promising, but not yet clinically applicable.

Pathophysiology of CDS

Multiples studies of the senior feline and canine brain highlighted a decrease in cerebral vascular blood flow, microbleeds or infarcts of periventricular vessels, and arteriosclerosis.[1,3,4] The compromised cerebral blood flow and damage caused by chronic free radicals (oxidative stress) can drive the pathophysiology of CDS in addition to the aforementioned changes in brain metabolism. The relative reduction in oxygenation of the brain tissue can be aggravated by an age-related decreased cardiac output, hypertension, and anemia. Due to their high metabolic rate, neurons are prone to hypoxic damage. The aging mitochondria become less effective in energy production and need readily available energy sources, which are, as previously

Table 1. Summarizes potential nutritional approaches for CDS in dogs; some solutions may be available as a functional ingredient or supplement in certain regions. Some supplements and functional ingredients are not available in all countries because of regulatory constraints.[1,3,4] Supplements should be evaluated for quality and safety.

Risk factors	Functional ingredient	Potential benefit
Glucose hypometabolism	MCTs	Increases ketones, alternative source of energy
Mitochondrial dysfunction	L-Carnitine	Improved mitochondrial function and mitochondrial lipid metabolism
Mitochondrial dysfunction	DL-alpha-lipoic acid*	Improves mitochondrial function; cofactor for mitochondrial respiratory chain enzymes
Oxidative stress (free radical damage)	Vitamins C and E, ß-carotene, selenium, flavonoids, carotenoids	Protects brain against oxidative stress
Altered neurotransmitter levels	S-adenosyl–L-methionine (SAMe)	Rebalances monoamine neurotransmitter level, cell membrane integrity
Chronic inflammation	DHA and EPA	Anti-inflammatory
DHA or phosphatidylserine deficiency	DHA or phosphatidylserine	Supports brain function and structure
Hypertension	Arginine (nitric oxide-releasing compound)	Improves blood pressure and blood circulation
High homocysteine	B vitamins	Prevents high homocysteine associated with cognitive impairment
Low B6, B12, folate	B vitamins	Supports energy metabolism, DNA maintenance, biosynthesis of neurotransmitters

*toxic in cats

mentioned, different than in young animals. Similar to people with Alzheimer's disease, dogs and cats form amyloid β-plaques and tau fibrils in CDS, but their relationship to its severity has yet to be clearly established.

DIETARY CONSIDERATIONS FOR CDS MANAGEMENT

Dietary management together with environmental enrichment build the cornerstone in CDS management, whereas prescription drugs currently play a minor role. There are commercially available diets for dogs with CDS, but not for cats. Dogs fed complete and balanced commercial diets suitable for the individual patient's life stage, body condition, and size are around three times less likely to be affected by CDS later in life.[1] The current dietary approaches mainly aim to improve mitochondrial function and health and reduce free radicals and inflammation (**Table 1**). Diets enriched with medium-chain triglycerides (MCTs) provide a source of MCFAs and ketones that can serve as alternative energy sources to glucose, and have shown promise in reducing clinical signs of CDS and

improving brain function in senior dogs (**Figure 1**).[2] A further study showed an improvement in signs of CDS when dogs were fed a diet with a "brain protection blend" composed of arginine, antioxidants (vitamins C and E, and selenium), B vitamins, and fish oil (as a source of the omega-3 fatty acids docosahexaenoic acid [DHA] and eicosapentaenoic acid [EPA]).[1,4] A similar improvement in CDS signs was reported in dogs on a diet containing fatty acids, antioxidants (vitamins C and E, ß-carotene, selenium, flavonoids, carotenoids), and mitochondrial cofactors (DL-alpha-lipoic acid and L-carnitine) (Table 1).[1]

EPILEPSY – CLINICAL CONSIDERATIONS

Epilepsy is defined by recurrent epileptic seizures.[9] However, epilepsy is a brain disease and has been also associated with neurobehavioral and cognitive comorbidities such as anxiety, attention deficit hyperactivity syndrome, reduced trainability, and cognitive dysfunction.[10]

Dietary Considerations for Epilepsy

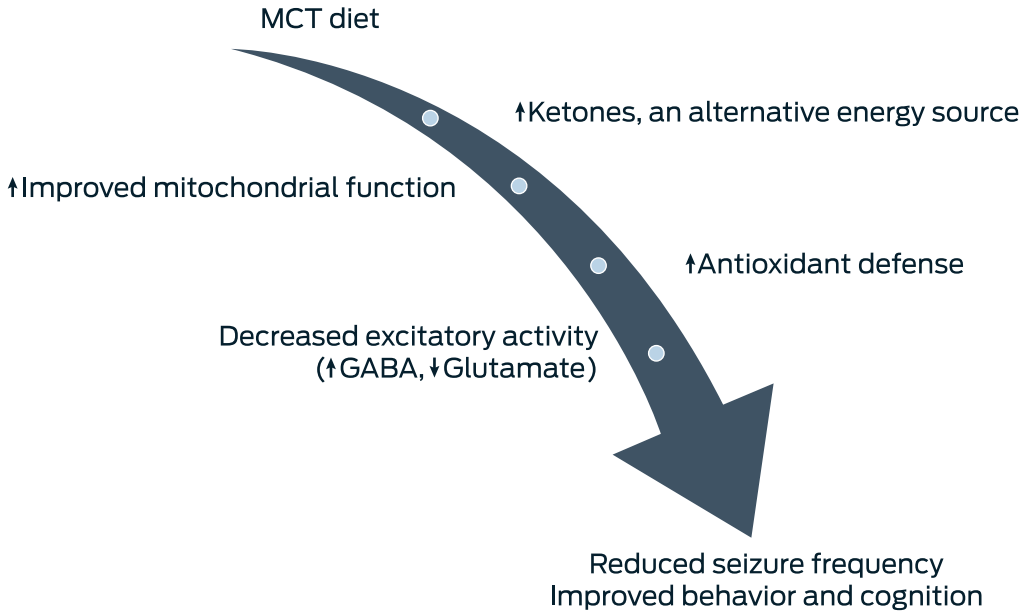
Antiseizure medications build the cornerstone for a successful management of a patient with epilepsy. However, two out of three owners will change the diet of their pet with the intention to improve seizure control and protect the animal from the adverse effects of the medication.[11] During a seizure, the body and the brain are under "stress," requiring readily available energy. Glucose metabolism significantly increases during the seizure, especially in the epileptic focus. Interictally, however, the opposite occurs: the brain areas causing seizure generation and propagation, morphologically altered or not, can be in a hypometabolic state with reduced glucose metabolism and mitochondrial function.[2] The area affected by hypometabolism can expand over time associated with an increase in epilepsy severity, implying that changes in metabolism and energy deficiencies might drive epileptogenesis and severity of epilepsy. The energy deficit and glucose hypometabolism could lower the seizure threshold by changing cell membrane potentials, glutamate transporter and synaptic activity. Furthermore, these hypometabolic regions, often affecting the hippocampus, amygdala, and other limbic brain structures, could explain the aforementioned comorbidities such as anxiety and cognitive dysfunction.[2] Similar to CDS, epilepsy management requires a strategy to overcome the alteration in glucose metabolism. This highlights the need for treatment strategies to improve brain energy metabolism and provide alternative energy sources.

As glucose metabolism is disrupted in epilepsy patients, ketones offer an alternative energy source. Ketones cross the BBB easily and can be utilized effectively in the affected brain regions. The classic ketogenic diet, in which three-quarters of the energy requirement is provided by LCFAs, is effective for the treatment of drug-resistant epilepsy in children. However, a classical LCFA-based ketogenic diet is not recommended for dogs with epilepsy because dogs are more resistant to nutritionally induced ketosis. A study in drug-resistant dogs with epilepsy using a classic LCFA-based ketogenic diet failed to replicate the success seen in people. Despite seeing a trend in seizure reduction in drug-resistant canine epilepsy patients with a high LCFA-based diet, the risk of dogs developing pancreatitis increased.[2,5] MCT-enriched diets provide a safer and more effective way of increasing serum ketones, as well as potentially supplying MCFAs for metabolism in the brain (Figure 1). Multiple trials with MCT-enriched diets in dogs with severe idiopathic epilepsy demonstrated that around 20–50% of dogs with antiseizure drug-resistant epilepsy respond adequately with a more than 50% reduction in seizure frequency.[2] Adverse effects (such as ataxia and sedation), and epilepsy comorbidities (such as anxiety, attention deficit hyperactivity syndrome, and cognitive impairment) improved in some of these dogs. To date, no significant adverse effects have been reported for MCT diets in dogs with epilepsy. Recently, however, a Cavalier King Charles Spaniel was described that had focal seizures and obtundation secondary to a gene mutation encoding medium-chain acyl-CoA dehydrogenase (MCAD), resulting in a more than 40-fold increase of the acylcarnitine C8/C12 ratio.[12]

COMMUNICATION TIP

"Nutritional strategies can improve brain function in health and disease."

Figure 1. Simplified schematic diagram of medium chain triglycerides (MCTs) mechanism of action, explaining its positive effect on epilepsy and cognition. MCTs provide an alternative energy source via increase of ketones, and improve mitochondrial function, antioxidant defense, and GABA/Glutamate ratio.



Therefore, metabolic testing of dogs presenting with unusual behavior and seizure pattern is recommended.

There is solid evidence to recommend MCT-enriched diets for canine epilepsy management,[13] but there is currently no data for cats and therefore no clear recommendation. When managing dogs with epilepsy, several other considerations are required, including body condition, dietary macronutrient distribution, serum trace nutrient concentrations, the possible role of food hypersensitivities, and dietary chloride intake in a dog on potassium bromide, as an increased chloride intake can reduce bromide uptake and increase its clearance.[2,5,13] The often-hyped role of gluten hypersensitivity in canine epilepsy has not been scientifically proven. However, there is a documented link between gluten hypersensitivity and certain movement disorders such as paroxysmal dyskinesia.[14] In dogs with paroxysmal dyskinesia, a gluten-free diet can improve clinical signs significantly.[15,16]

CONCLUSIONS

Nutritional strategies can improve brain function in health and disease. There is a moderate level of evidence for dogs, but not for cats, for different dietary approaches that can improve cognitive dysfunction and epilepsy. Current nutritional management for these diseases aims to maintain or improve brain energy supply, modulate disease risk factors such as oxygen free radicals, inflammation, and altered blood supply, and improve behavioral comorbidities. More long-term studies are needed to elucidate potential mechanisms of action and the role of nutritional management for routine patients not only for the dog, but especially for the cat.

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BEHAVIORAL DISORDERS IN DOGS AND CATS

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KEY TAKEAWAYS

- The causes of behavioral disorders are multifactorial and often include physical disorders.
- Functional dietary ingredients and supplements can be effective at reducing fear, anxiety, and stress and improving cognition.
- Feeding management changes can also affect the behavior patterns of companion animals.

DEFINITION

Behavioral disorder is an expansive label including disorders of fear, anxiety, stress, conflict, panic (FASCP), impulsivity, phobia and undesirable behaviors. Anxiety is a generalized response in anticipation of a threat that is not present. Fear is a targeted response to a threat that is present.

Across the globe, behavioral problems in companion animals are common, occurring in approximately 85% of dogs[1,2] and 75% of cats.[3] In the United States, up to 20% of dogs have separation-related disorders (SRD), 41% exhibit aggression,[4,5] and up to 50% suffer from noise aversion.[4-6] Dogs with fear and anxiety disorders are at increased risk of skin disease and reduced longevity.[7] Both dogs and cats with behavioral disorders are at significant risk of relinquishment and euthanasia.[8]

KEY DIAGNOSTIC TOOLS AND MEASURES

Behavioral clinical signs may result from changes in any body system. As such, behavioral assessment and treatment start with a complete physical assessment for pain and discomfort,[9,10] nutritional assessment and a behavioral history. Brief history forms for use in primary care practice are readily available online. Validated questionnaires are also available.[11-17] A minimum database should be collected on all pets presenting with behavioral signs including physical examination, CBC, serum chemistry, urinalysis, fecal antigen testing including giardia, thyroid assessment, and nutritional assessment (i.e., complete diet history).

PATHOPHYSIOLOGY

Factors that affect behavior: The development of behavioral disorders is influenced by genetics, epigenetics, coping style, environmental experience, and learning. Maintenance of behaviors occurs through positive and negative consequences which immediately follow the target behavior and may be extrinsic (e.g., owner-dependent) or intrinsic (e.g., dissipation of fear, anxiety, stress, conflict, panic, pain or discomfort). In cases where behavioral signs are influenced or caused by physical disorders, behavioral signs may persist after resolution of the primary medical problem.

Neurotransmitters and diet: The emotional states (FASCP) which drive behavior patterns are accompanied by physiologic responses involving, but not limited to, neurotransmitters and hormones. The stress neurotransmitters that can potentially be manipulated through diet are GABA, glutamate, serotonin, norepinephrine, epinephrine and dopamine. Changes in these neurotransmitters have been associated with aggression in some animals.[18]

The amount of nutrient ingested, the amount that reaches the brain, and the final concentration of the neurotransmitter synthesized are not necessarily linearly correlated. The amount of neurotransmitter synthesized is dependent on the availability of circulating precursors, the ratio of precursors to other large-chain amino acids (large neutral amino acids, LNAA) (e.g., tryptophan), ratios of macronutrients (e.g., carbohydrates, protein) and the transporters which move precursors to synthesis sites.

Food sensitivities/intolerance: In dogs, behavior changes alone can be the sole clinical sign of an adverse food reaction such as nonceliac gluten

hypersensitivity,[19] however they may accompany more localized gastrointestinal signs such as plant eating and vomiting.[20]

Alterations in feeding schedule or method: Changes to feeding schedule or method can increase FASCP leading to aggression and irritability. Calorie restriction may increase anxiety and conflict around eating and mealtime.

Gut microbiome: In dogs, differences in gut microbiome have been associated with changes in aggression, anxiety and memory performance.[21-23] In addition, the gut microbiome plays a role in the production of monoamine neurotransmitter precursors and GABA, which modulate fear, anxiety, aggression, hypervigilance, muscle tension and stress.[24]

Essential fatty acids: There is evidence that dogs with some types of aggression may have serum lipid profiles which are significantly different than non-aggressive dogs.[25] In addition, lower docosahexaenoic acid (DHA) concentration and a higher omega-6/omega-3 ratio may be more common in some aggressive dogs.[26] Dogs with attention deficit hyperactivity disorder-like behavior were found to have lower serum phospholipid levels and higher arachidonic acid levels.[27]

Vitamins: Neurotropic B vitamins include B1 (thiamine), B3 (nicotinamide), B6 (pyridoxine) and B12 (cobalamin).[28] Vitamin B1 plays a part in the maintenance of nerve membrane function, energy metabolism, and in synthesis of myelin, acetylcholine, serotonin and amino acids.[29] Vitamin B3 has effects on serotonin and GABA.[30] Vitamin B6 aids in the production of serotonin, GABA, and norepinephrine; and has neuroprotective qualities.[31] Vitamin B12 acts as a cofactor in biochemical processes intended to maintain nervous system health.[31,32]

SIGNALMENT

Behavior disorders can affect any breed of dog or cat at any age. Signs of cognitive dysfunction may start as early as 7 years of age in dogs. Bull Terriers and German Shepherd Dogs are more likely to present for tail chasing or spinning.[33] Burmese and Siamese cats are more likely to present with pica.[34] Breeds selected for cooperative work with humans such as Weimaraners may be predisposed to separation-related disorders.[35]

KEY NUTRIENT MODIFICATIONS

Behavioral disorders resulting solely from changes in diet and food intolerance have been reported.[19] In these cases, nutritional changes may be curative. However, more often treatments such as the ones below do not "cure" behavioral disorders, but instead lower the pet's stress – thus decreasing the target behavior and facilitating implementation of behavioral treatments. Each family will have unique needs, abilities and resources which can be dedicated to the treatment of the pet's behavioral disorder. Variability in treatment adherence contributes to variability in the likelihood of discontinuation of the nutritional interventions. Pets should be fed therapeutic diets, additional nutrients or supplements for 45–60 days before decisions can be made regarding their effect on the target behavior. Even then, some positive effects may take longer to become apparent.

Alpha-casozepine: Alpha-casozepine is a trypsin hydrolysate of alpha S1-casein, a protein found in cows' milk that binds at the GABA-A receptor.[36] In dogs and cats (with behavior modification) alpha-casozepine given on a daily basis has been shown to reduce anxiety.[37,38] Alpha-casozepine is available in several commercial diets or as a supplement. When fed in a commercial diet, alpha-casozepine has been shown to lower cortisol in stressed dogs compared to a control diet.[39] In cats exposed to the stress of a veterinary visit, 75 mg/kg PO q24 for 3 days had a mild effect on the stress level. See **Table 1** for dose ranges.[40]

Carbohydrate: Tryptophan competes with other LNAA for transport through the blood–brain barrier (BBB), described below in more detail. A preliminary study suggested that a high-carbohydrate, protein-free meal may increase tryptophan concentrations in the brain, presumably as a result of insulin secretion moving LNAAs into the muscle, which removes competition and allows tryptophan to enter the brain more easily.[41] However, no correlation has been found between dietary carbohydrate concentration and behavior, including aggression, and serum levels of cortisol, tryptophan, and serotonin.[42,43]

Fatty acids: Older Beagles fed a proprietary diet supplemented with DHA for 25 weeks showed improved initial learning on contrast discrimination tests, however long-term recall of the task did not change with treatment.[44]

Table 1. Recommended evidence-based doses of possible behavioral supplements for both dogs and cats

Ingredient	mg/kg PO	Dosing frequency
L-theanine	5-10	Twice daily, or 3 hours prior to events
Alpha-casozepine	15-30 75	Once daily Once daily for 3 days prior to the onset of stressful events

L-theanine: L-theanine is an amino acid that acts as a glutamate receptor antagonist and increases GABA, resulting in inhibitory and relaxing effects. It may increase serotonin and dopamine in specific brain areas. Several studies in dogs support an effect of L-theanine in reducing noise fears and phobia, storm-related anxiety, and fear of unfamiliar people over 4–8 weeks of twice daily treatment.[45-47] In cats, supplementation with L-theanine for 30 days significantly improved stress-related signs including hypervigilance, nervousness, fear and undesirable elimination.[48] See Table 1 for dose ranges.

Medium chain triglycerides (MCT): Supplementation with MCT can result in higher levels of ketone bodies in dogs, which may provide an alternative energy source for the aging brain as glucose metabolism declines.[49] Dogs fed 5.5% MCT on an as fed basis for 2 weeks demonstrated fewer errors on learning tasks when compared with controls; however, more significant differences were seen after 1 month of supplementation.[49] Significant differences in executive function (reasoning) were seen between the control and treatment groups after 3 months on the diet, and after 6 months there were differences in focus and attention demonstrated between the groups. Cognitive dysfunction syndrome is discussed under Brain Disorders and elsewhere in this book.

Probiotics: *Bifidobacterium longum* BL999, administered to dogs for 6 weeks has been shown to be associated with a significant reduction in anxious behaviors including barking, jumping, spinning, and pacing; reduced salivary cortisol levels; a decrease in heart rate; and increased heart rate variability, indicating an improved emotional state.[50] Cats given BL999 daily for 6 weeks demonstrated a higher tolerance for stress when compared to cats receiving a placebo when tested over the following 6 weeks.[51] Dogs with existing behavioral disorders fed *Lactiplantibacillus plantarum* PS129 daily for 2 weeks were less aggressive and less anxious (when alone). Additionally, dogs with separation anxiety had decreased plasma serotonin turnover rates, implying positive changes in serotonin metabolism.[52]

Protein: Dogs fed diets with 17% and 25% protein on an as fed basis for 2 weeks demonstrated a decrease in territorial aggression compared with their behavior when fed a diet with 32% protein, but there were no differences regarding other types of aggression or hyperactivity.[53] In a later study in dogs, one week of feeding a diet with 18% protein on an as fed basis containing 3 g of tryptophan per kg food reduced territorial aggression in dogs with a fear component, but had no effect on hyperactivity and owner-directed aggression.[54] In the same study, dogs fed a diet with a protein concentration of 30% and 2.4 g tryptophan per kg food showed increased owner-directed aggression.

Tryptophan: Tryptophan is the precursor of serotonin and melatonin. In order to increase the rate of synthesis of serotonin via oral tryptophan supplementation, a dietary tryptophan:LNAA ratio of 0.061:1 has been suggested as ideal to decrease competition between tryptophan and other LNAA for a common carrier to cross the blood-brain barrier (BBB).[55,56] Without crossing the BBB, tryptophan cannot be used for serotonin synthesis and has no effect on neurotransmitters. The majority of studies thus far assessing tryptophan supplementation in dogs and cats for behavioral change have shown little to no effect.[55,57] However, in one study, supplementation with L-tryptophan led to a reduction of stress-related behaviors and a decrease in anxiety signals in both dogs and cats.[58]

Tyrosine: Tyrosine is the precursor of dopamine, norepinephrine and epinephrine. In one study of Labrador Retrievers, Toy Poodles and German Shepherds, 100 mg/kg of tyrosine fed daily for 3 days decreased the time needed to acquire a new behavior and the reaction time to the cue given for some dogs.[59]

Combination Products

Commercial diets: Tryptophan and alpha-casozepine are frequently combined as functional dietary ingredients and are included in several commercial diets. Dogs fed a diet supplemented with both alpha-casozepine (1.35 g/kg) and L-tryptophan (3.04 g/kg) for 8 weeks had lower urine cortisol to creatinine ratios following a visit to the veterinary hospital and a toenail trim.[60] Cats fed the same diet for 4 weeks showed decreased fear in a new place, but not with a new person.[61] Cats fed a diet with 3.6 g/kg of tryptophan (tryptophan:LNAA = 0.037) and 15 mg/kg of alpha-casozepine for 8 weeks had lower urine cortisol to creatinine ratios, however there was no effect on stress during a veterinary examination and blood draw.[62] Cats with a history of feline lower urinary tract disease (FLUTD) fed a veterinary therapeutic diet for 6 weeks demonstrated higher quality of life scores as assessed by the owner and positive changes in clinical signs of FLUTD.[63]

COMMUNICATION TIP

"It is common to institute several types of treatment including environmental management, behavior modification, nutrition, and pharmaceuticals to help lower stress."

Several diets have shown promise in alleviating the signs of cognitive impairment or dysfunction in dogs and cats. A commercial diet with 6.5% MCT on an as fed basis and a targeted nutrient blend (DHA, EPA, vitamin E, vitamin C, B vitamins, arginine) fed for 90 days reduced the behavioral signs of Canine Cognitive Dysfunction Syndrome (CCDS).[64] A diet containing a proprietary blend of antioxidants and mitochondrial cofactors has been shown to improve cognition in senior dogs.[65] Cats fed a diet containing a targeted nutrient blend (EPA, DHA, arginine, alpha-tocopheryl acetate, vitamin C, selenium, thiamine, riboflavin, pantothenic acid, pyridoxine, cyanocobalamin, and folic acid) fed over 1 year showed significant improvements in learning after 30 days and potential neuroprotective effects after one year.[66]

Commercial supplements: A proprietary blend of the extracts of *Magnolia officinalis*, *Phellodendron amurense* and honokiol has been shown to reduce thunderstorm fear in dogs after 7 days of treatment at label dose.[67] A similar product with L -theanine, *Magnolia officinalis*, *Phellodendron amurense*, and whey protein concentrate when administered to shelter dogs for 9 days had no effect on fecal cortisol level and positively affected only one behavioral parameter (light sleep).[68]

RECOMMENDED RANGES OF KEY NUTRIENTS

For most supplements, there are no published doses. The ingredients or nutrients for which there are doses published are listed in Table 1. All doses are for both dogs and cats.

THERAPEUTIC FEEDING PRINCIPLES

The foundation of the treatment of behavioral disorders in dogs and cats is the reduction of FASCP. Where available and indicated, recommend that clients feed complete and balanced diets with added ingredients or supplements from trusted manufacturers to reduce stress instead of purchasing ingredients and supplements with lack of knowledge of quality control. The amount of the diet fed will affect the amount of the nutrient or ingredient that is digested and available for anxiety relief and neurotransmitter production. Dogs and cats may become more irritable and/or aggressive when placed on weight loss plans, even when the energy requirement is consistent with the calories being fed. Use of food and puzzle toys as well as low-calorie treats at less than 10% of total daily calories can help to keep the pet satiated and avoid behavior changes. Additional client education points are shown in **Box 1**.

COMMON COMORBIDITIES

Separation-related disorders commonly occur with noise and storm fear or phobia.[69] Systemic disease and orthopedic pain are common in dogs presented to veterinary behaviorists for behavioral disorders.[10] Endocrine disorders such as hyper- or hypothyroidism commonly have associated behavioral signs.[70] Dogs who present later in life (6.5 years or older) with a primary complaint of noise aversion are more likely to have contributing orthopedic disease.[71]

Box 1. Client education points

- Use food and puzzle toys to increase the time that it takes to consume meals, prolonging mealtime and increasing enrichment. Enrichment with food can decrease stress and also may increase the energy expended while eating and reduce the amount eaten at each meal.
- When feeding a diet with an ingredient to help reduce anxiety, the amount of the ingredient the pet receives will be affected by how much of the diet they are given. Feeding less of the diet will reduce the ingested amount of the active ingredient.
- Try to keep feeding schedules the same each day to reduce anxiety.
- Do not change feeding management factors (including the schedule, bowl, etc.) abruptly.
- Only use science-based dietary supplements produced by trusted manufacturers.

INTERACTING MEDICAL MANAGEMENT STRATEGIES

Supplementation with tryptophan should be used with caution if combining with medications that affect serotonin to avoid serotonin syndrome.

MONITORING

Patients with behavioral disorders benefit from regular veterinary healthcare team member follow up at 1- to 2-week intervals for the first 8 weeks.

The best outcomes when treating behavioral disorders are achieved through:

1. Assessment of overall wellness.
2. Medications, diet changes and/or supplements used to change the body's response to FASCP.
3. Environmental changes to reduce the opportunities to exhibit the target behavior.
4. Science-based behavioral treatments which address FASCP and aid in the acquisition of coping skills.

CONCLUSIONS

Clinical signs which are characterized as behavioral can indicate deficits, diseases and disorders of any body system. As such, a holistic approach is necessary for the best patient outcome. Evaluation of overall wellness (pain, discomfort, inflammation, infection, nutrition) is the first step. Behaviors which are reinforced often will continue to be exhibited even when the primary cause is resolved. For that reason, it is common to institute several types of treatment including environmental management, behavior modification, nutrition, and pharmaceuticals to help lower stress. Therapies which alleviate FASCP and reduce the target behaviors should not be delayed during the health and wellness assessment. Treatments may be needed for a short-term period until clinical signs and the target behavior are resolved or they may be necessary for the life of the pet.

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PRACTICAL TOOL: ASSESSMENT TOOLS FOR COGNITIVE DYSFUNCTION SYNDROME IN DOGS

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Canine Cognitive Dysfunction Syndrome (CCDS) is a degenerative neurobehavioral disorder of aging dogs characterized by impairments in mentation and behavior changes, akin to human Alzheimer's Disease. ß-amyloid deposits, vascular damage, and other neuropathologic changes can be detected on histopathology. A more thorough discussion on clinical signs and associated pathologies is found in the chapter Brain Disorders in Dogs and Cats. No definitive pre-mortem diagnostic tools are available for CCDS at this time, although neurodegenerative biomarkers are showing promise. Currently, clinical diagnosis is based on 1) assessment of medical conditions that may mimic or contribute to cognitive decline, and 2) scoring on a caregiver-queried behavioral questionnaire. Treatment options, including nutraceuticals, pharmaceuticals, and enrichment activities, aim to enhance cognitive abilities and improve quality of life.

Dogs in the last 25% of their breed's predicted lifespan, which is approximately 7–8 years of age, should be examined every 6 months, and a minimum laboratory database is recommended at each visit.[1] A minimum database for senior dogs should also include a thorough behavioral history and questionnaire responses, as well as a diet history (**Figure 1**). Clinical signs or laboratory findings may warrant additional laboratory diagnostics, imaging, and/or therapeutic trials. The most successful treatment outcomes result from addressing all comorbidities, including any source of pain or discomfort.

There are many published questionnaires designed to assess the cognitive status of aging dogs. The Canine Dementia Scale (CADES)[2] and Canine Cognitive Dysfunction Rating (CCDR) scale[3] are examples of more comprehensive and partially validated tools. Additional tools exist, some of which may be easier for veterinary teams to implement with limited appointment times. The DISHAA (**D**isorientation; Social **I**nteractions; **S**leep–Wake Cycles; **H**ouse-soiling, Learning and Memory; **A**ctivity; and **A**nxiety) tool[4] and CCAS (Canine Cognitive Assessment Scale)[5] are examples of less comprehensive scoring assessments that are easier to implement. Some of the differences between these tools are shown in **Table 1**. All of the questionnaires can screen for the presence of impairments within similar domains (e.g., spatial orientation and social interactions). CCDR, DISHAA, and CCAS are intended to be completed by the dog's caregiver alone. As conditions other than dementia may impact caregiver evaluations on the scoring tools, the CADES was designed to be administered by a veterinarian along with the caregiver to better identify significant clinical signs and improve response objectivity. CCDR and CADES provide a stratification of severity, although all tools can provide some evaluation of disease progression over time. It is important the same tool be implemented when longitudinally tracking clinical signs.

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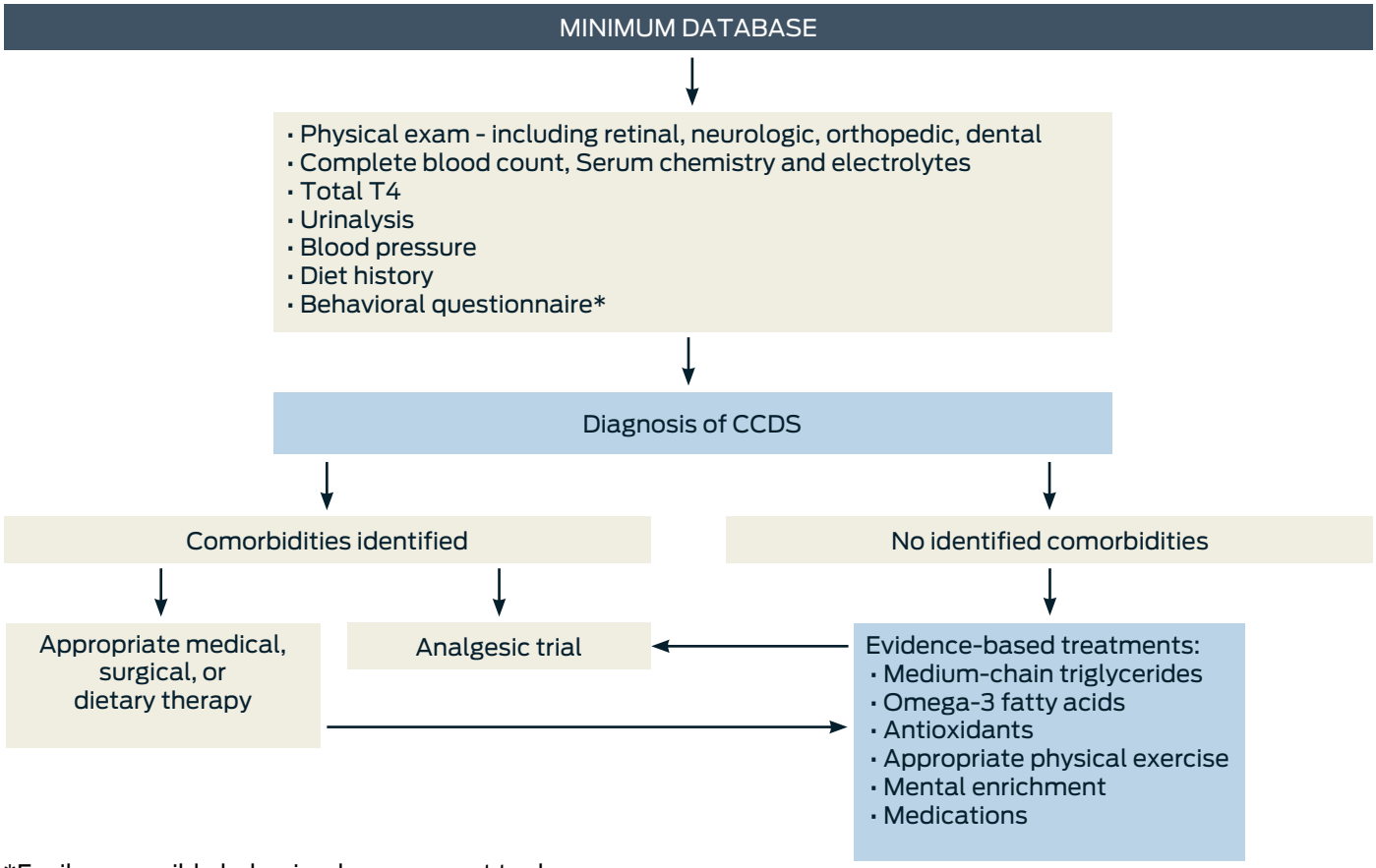
Figure 1. Management of suspected canine cognitive dysfunction syndrome



*Easily accessible behavioral assessment tools

Table 1. Example behavioral tools for the assessment of canine cognitive dysfunction syndrome

	Evaluates cognitive and behavioral domains associated with CCDS & provides trackable score	Recommended completion by	Features
Canine Dementia Scale (CADES)[2]	Yes	Patient Caregiver + Veterinarian	More comprehensive, partially validated
Canine Cognitive Dysfunction Rating Scale (CCDR)[3]	Yes	Patient Caregiver	More comprehensive, partially validated
DISHAA cognitive dysfunction assessment tool[4]	Yes	Patient Caregiver	Less comprehensive, easier to implement
Canine Cognitive Assessment Scale (CCAS)[5]	Yes	Patient Caregiver	Less comprehensive, easier to implement

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CARDIAC DISEASE

CARDIAC DISEASE IN DOGS

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KEY TAKEAWAYS

- Heart disease in dogs requires frequent monitoring and an individualized diet plan that adjusts with the needs of the patient.
- Although dietary changes may not be necessary for all stages of heart disease, feeding a complete and balanced diet that supports a healthy body condition is an important element of supporting long-term health.
- Understanding which nutrients are important in supporting dogs with heart disease can improve outcomes.

OVERVIEW

Myxomatous mitral valve disease (MMVD) is one of the most common forms of heart disease in dogs.[1,2] Studies have reported increased prevalence in Dachshunds and Cavalier King Charles Spaniels.[3] The disease is characterized by nodular thickening and expansion of the spongiosa layer within the mitral valve and tricuspid valve leaflets.[1,4] Although the mechanism is not fully understood, one proposed mechanism of this degenerative condition involves glycosaminoglycan deposits within the valves rather than inflammation.[4] The thickened valves do not close properly, resulting in valvular regurgitation which creates an audible murmur; as a result, auscultation is the most practical screening tool for MMVD with echocardiogram being a more sensitive test.[5] Due to the slow, yet progressive nature of this disease, radiographic changes may take several years to develop following detection of a murmur. Biomarkers such as brain natriuretic peptide (BNP) may aid in monitoring the severity of mitral valve disease.[6] BNP is released with injury and remodeling of the cardiac muscle and can be detected by measuring the N-terminal portion of pro-brain natriuretic peptide (NT-proBNP). Increases in NT-proBNP indicate cardiac changes that may help identify patients at an increased risk for congestive heart failure; however, not all dogs that develop CHF will have an increase in NT-proBNP.[6,7] Although dogs with MMVD can remain nonclinical for many years, acute congestive heart failure can develop in the event of a ruptured chordae tendinea, which is a known complication associated with MMVD.[8] Other forms of heart disease such as dilated cardiomyopathy (DCM) can also occur in dogs. DCM involves ventricular and cardiac enlargement that results in impaired systolic function and can lead to congestive heart failure, arrhythmias, or a combination of the two. Large and giant breed dogs are overrepresented, but it is also seen in spaniel breeds. DCM is associated with an autosomal dominant trait in Doberman Pinschers, Boxers, Irish Wolfhounds, and Newfoundlands. The US Food and Drug Administration (FDA) Center for Veterinary Medicine has been investigating a potential link between nutrition and DCM in dogs. Veterinarians and pet owners wishing to learn more about the FDA investigation on DCM should refer to www.fda.gov. This chapter will focus on nutritional management of MMVD.

The American College of Veterinary Internal Medicine (ACVIM) created a staging system for MMVD and heart failure as well as guidelines for treatment at each stage (**Table 1**).[9] Regardless of the stage of disease, a thorough nutritional assessment of every patient is encouraged, followed by individualized diet recommendations; however, ACVIM does not recommend dietary change to manage the heart disease until stage B2.

DIET

When considering nutritional management of cardiovascular disease, a key priority is to feed a complete and balanced diet that will support a healthy body condition and minimize the loss of lean body mass (**Table 2**). As heart disease advances, there is a loss of lean muscle mass, termed cardiac cachexia, which is associated with a poorer prognosis. Cachexia is multifactorial and involves increased inflammatory cytokines, oxidative damage, inadequate delivery of nutrients, and impaired clearance of metabolic waste

Table 1. ACVIM staging system for MMVD and heart failure[9]

Stage A	Dogs at risk for developing heart disease, but no identifiable changes
Stage B	Dogs with signs of heart disease (e.g., murmur) but do not have clinical signs of heart failure
Stage B1	Asymptomatic dogs that do not have radiographic or echocardiographic cardiac changes
Stage B2	Asymptomatic dogs with mitral valve regurgitation associated with cardiac remodeling
Stage C	Dogs with either current or past clinical signs of congestive heart failure related to MMVD
Stage D	Dogs with severe clinical signs of heart failure that are refractory to treatment

products. Although negative energy balance is one potential cause for loss of lean body mass, it is not the only factor and as such cannot be easily reversed by increasing calories. It is for these reasons preservation and maintenance of body weight and muscle mass are important to address early in the disease process. Although ACVIM guidelines do not indicate dietary changes are necessary in dogs diagnosed with Stage A or Stage B1 heart disease, it is the ideal stage to ensure the patient is eating a complete and balanced diet and maintaining lean body mass as well as a healthy body condition. Identifying a diet that the patient is willing to eat at early stages of heart disease but also appropriate for more advanced stages is beneficial. Treats and human food can be high in sodium, which can be deleterious to dogs with more advanced disease. Discussing treat options early in the disease process provides owners the opportunity to identify safe treats that their pet enjoys. A complete diet history helps identify sources of food that may add excess calories or increase the risk for malnutrition. Calories coming from treats and human food should provide less than 10% of the total daily caloric intake to avoid malnutrition. Assessing whether the dog has had a selective appetite in the past allows the veterinarian to explore whether there are other comorbidities that may explain inappetence, such as adverse food reaction or chronic enteropathy. Pet owners that have a dog with a selective appetite may top-dress the dog's food with a variety of food or treats to keep their dog interested in eating. Providing guidance to pet owners regarding the appropriate type and amount of food during the early stages of heart disease reduces the risk for complications that could occur as disease progresses. There is evidence that suggests modifying the diet early in the disease process may help promote heart health. In a randomized controlled pilot study, dogs with Stage B1 and B2 MMVD fed a cardiac protection blend of nutrients had a decrease in left atrial size and reduced mitral regurgitation compared to dogs fed a control diet without the cardiac protection blend.[11]

NUTRIENTS

Palatability and Digestibility

Many dogs with advanced heart disease will experience a decreased or loss of appetite. This may be related to their disease but can also be a side effect from medications commonly used in management of heart disease. Finding ways to enhance palatability by offering low-sodium toppers such as honey, maple syrup, baked skinless, boneless chicken breast, vegetables, fruit, or low-fat yogurt may promote acceptance of the diet. To avoid the risk of malnutrition, treats and toppers should not exceed 10% of total daily caloric intake. When feeding dogs food that is intended for people, it is important to screen for the presence of ingredients toxic to dogs, including xylitol or birch sugar, which are artificial sweeteners that can lead to hypoglycemia and hepatic damage.

Heart failure is complex syndrome affecting numerous body systems. As heart disease progresses, compromised blood flow to the digestive tract may adversely affect digestive function, and highly digestible diets may improve absorption of nutrients in these patients. Congestive heart failure can lead to changes of the intestinal barrier function and alterations in gut microbiome, which may result in impaired absorption of nutrients from the intestines; therefore, feeding a highly digestible diet is recommended. Including prebiotics in the diet can support a healthy microbiome;

Table 2. Nutrition guidelines for MMVD

Stage A no formal recommendation	· Feed complete and balanced diet that supports a healthy body condition
Stage B 1 no formal recommendation	· Feed complete and balanced diet that supports a healthy body condition
Stage B2 mild sodium restriction (<100 mg/100 kcal)[10]	· Feed a complete and balanced diet · Provide adequate calories and protein for optimal body condition · Determine what type of palatability enhancers the patient might enjoy
Stage C/D modest sodium restriction (<75 mg/100 kcal)	· Feed a complete and balanced diet · Feed highly palatable diet · Prevent cachexia – maintain adequate calories and protein – consider omega-3 fatty acids – monitor for nutrient excess and deficiencies

however, more work is needed to determine the optimal blend of fiber including prebiotics in patients with heart disease.

Protein

Protein restriction was recommended at one point because there was a concern that high-protein diets would increase the "workload" on the liver and kidneys; however, we understand now that protein restriction is not indicated unless there is a comorbidity such as renal disease. Unnecessary protein restriction can lead to loss of lean body mass and malnutrition. Nitrogen balance has been used as a method to determine if protein needs are being met; however, dogs maintaining their nitrogen balance can experience a loss of lean body mass, and minimum protein requirements in aging healthy dogs based on nitrogen balance may not be adequate.[12] Dogs with CHF often experience a loss of lean body mass and have increased metabolic demands and therefore may benefit from more protein than AAFCO and FEDIAF minimum requirements as long as they do not have renal disease. In the author's experience, diets that provide at least 5.5 g protein/100 kcal are often recommended (**Table 3**).

Taurine

Taurine is a sulfur-containing free amino acid that has inotropic and antioxidant properties. Dogs can synthesize taurine and therefore it is not considered an essential amino acid as it is in cats. However, it is important that the diet contains the necessary precursors for taurine synthesis. Cats fed a diet deficient in taurine have been shown to develop dilated cardiomyopathy (DCM) that can improve with taurine supplementation.[13] Similar reports exist in dogs, however more work is needed to determine the relationship between diet and DCM in dogs.[14] Dogs with MMVD and other heart diseases may benefit from additional taurine supplementation.

Box 1. Potential drug / nutrient interactions

- Loop diuretics can increase the risk for hypokalemia and hypomagnesemia
- Angiotensin-converting enzyme (ACE) inhibitors can increase the risk for hyperkalemia
- Azotemia can occur with diuretics
- Anorexia/hyporexia can be a side effect of cardiac medications (diuretics, digoxin, ACE inhibitors)

Fat

Fat provides the most calories per gram compared to the other macronutrients and can enhance palatability.

Dogs with heart disease often experience a loss of appetite and weight loss, both of which may benefit from increasing dietary fat as it can help support appropriate caloric intake. Long-chain polyunsaturated omega-3 fatty acids may be beneficial in dogs with heart disease and therefore, the type as well as the amount of dietary fat is important to consider. Chronic heart disease is considered an inflammatory condition with increased eicosanoid production.[15,16] Fish oil has a high concentration of omega-3 fatty acids that have been shown to decrease cytokine production, modulate inflammation, reduce the incidence of arrythmias, and improve cardiac cachexia.[17,18] The cardiac muscle requires a substantial amount of ATP to maintain normal function and, as a result, relies on fatty acid oxidation as a primary energy source. In humans with advanced stages of heart failure, enzymes in the myocardial cells that are responsible for energy metabolism are downregulated, and there is evidence that there is a change in substrate utilization from fat to glucose.[2,19] This results in decreased fatty acid oxidation and increased glycolysis and glucose oxidation to meet energy requirements. These changes may lead to poor contractility and ventricular remodeling. Medium-chain triglycerides (MCTs) have been evaluated as an alternate energy source because they do not require carnitine-mediated transport to cross the mitochondrial membrane, which allows MCTs to be easily absorbed and utilized.[11] In addition, MCTs can be metabolized to form ketones, which can be used as an alternative energy source within cardiac myocytes.[20]

Minerals

Sodium is important in the maintenance of blood volume because it is the primary osmotic agent in the extracellular fluid. The Renin-Angiotensin Aldosterone System (RAAS) is responsible for controlling sodium excretion and maintains sodium water balance in healthy dogs. In the case of heart failure, there is a drop in blood pressure, resulting in retention of sodium and water via RAAS in efforts to normalize the blood pressure. A consequence of RAAS activation is fluid retention that results in edema within the pleural space or abdomen. Diets formulated for heart disease are often sodium-restricted to address this; however, if the diet is too restricted in sodium, it may lead to early activation of RAAS.[21,22] Early and prolonged RAAS stimulation has been associated with increased inflammation and

Table 3. Nutrients of concern for cardiac disease in dogs

Calories	· Ensure adequate intake to maintain body weight and BCS
Protein	· High quality, highly digestible · At least 5.5 g/100 kcal to help maintain lean body mass
Fat	· Omega-3 fatty acids have anti-inflammatory and antiarrhythmic effects · Optimal dose not determined, although a dose of 40 mg EPA and 25 mg per kg body weight DHA has been suggested[10]
Sodium	· Control in diet and other sources of food · Early disease – mild sodium restriction: <100 mg/100 kcal · Mild to moderate disease – moderate sodium restriction: <75 mg/100 kcal
Potassium & Magnesium	· Monitor – serial evaluation may be useful · Diets will range in potassium content: evaluate diet and if patient is hypo- or hyperkalemic, make dietary adjustments as needed · Supplement magnesium in patients with hypomagnesemia
Antioxidants	· Many commercial diets contain antioxidants such as vitamin E, vitamin A, and selenium · Effect of antioxidant supplementation with CHF is unknown
B-Vitamins	· Supplementation may be beneficial in patients on diuretics

oxidative damage, exacerbation of clinical signs, and glomerular and vascular damage.[23] In human studies, excessive sodium restriction has been related to increased mortality.[24,25] Dogs on diuretics were found to tolerate a diet contained 40–70 mg/100 kcal of sodium; therefore, diets that provide at least 40 mg/100 kcal of sodium are recommended.[22]

COMMUNICATION TIP

"Demonstrating to the pet owner how to monitor for changes in respiratory rate and effort as well as changes in lean body mass and body condition can aid the pet owner in determining when they should seek veterinary care for their dog with heart disease."

Magnesium is important in normal cardiovascular function but can be challenging to accurately assess in patients because serum magnesium levels do not reflect body stores of magnesium. Despite this, it is important to monitor for low magnesium because magnesium below the reference interval may contribute to cardiac arrythmias and decreased myocardial contractility in dogs with heart disease. Diuretics can result in loss of magnesium and supplementation may be necessary in patients with hypomagnesemia. Although additional supplementation with magnesium may not be warranted in all dogs with heart disease, feeding a diet that is complete and balanced is an important component of every diet plan.

Potassium is important in acid base regulation and nerve signal transmission. Alterations in serum potassium can occur with the use of cardiac medication, and hyperkalemia can result in life-threatening arrythmias. Modification of dietary potassium should be implemented based on the patient's serum potassium levels, and frequent monitoring is recommended.

Other Nutrients

Dogs with heart disease can experience impaired cellular metabolism and inadequate oxygenation, which results in increased production of reactive oxygen species. Increased oxidative stress leads to cell damage and may exacerbate the development of and progression of cardiac disease.[26] Cellular antioxidants such as vitamin E and selenium are essential nutrients that also have anti-inflammatory properties. The dietary requirement for vitamin E can be influenced by the amount of polyunsaturated fatty acid (PUFA) in the diet. Additional vitamin E may be required when supplementing the diet with fatty acids.

Carnitine is important in cardiac function because it facilitates transportation of fatty acids into the mitochondria of myocardial cells. Carnitine also plays a role in calcium regulation and supports maintenance of the endothelium.[27] A carnitine deficiency can lead to alterations in fatty acid metabolism and has been associated with cardiomyopathy and cardiac arrhythmias in humans.[27] Carnitine can come from dietary sources or be synthesized endogenously if adequate methionine and lysine are present.

A complex interplay of nutrients emphasizes the need to feed a complete and balanced diet. As an example, the rate of carnitine utilization was accelerated in rats fed a diet low in choline.[28] This is relevant because choline has been determined to be one of the nutrients that fell below AAFCO requirements in dogs fed reduced calories on a weight loss plan.[29] Although calories are not restricted intentionally in dogs with heart disease, many dogs experience a cyclical appetite and will not always meet their resting energy requirements from their diet or may be fed a diet where >10% of the

Box 2. Monitoring tools for dogs with MMVD

- Body weight – remember fluid accumulation can mask weight loss
- Body condition score
- Muscle condition score
- Clinical signs – difficulty breathing, increased resting respiratory rate, weakness, syncope, gastrointestinal signs
- Laboratory values – BUN, creatinine, electrolytes, hematocrit
- Imaging as needed – thoracic radiographs, ECG, echocardiogram
- Blood pressure

calories are coming from an unbalanced food source. Dogs with insufficient caloric intake are not only taking in insufficient calories to maintain their weight but are also at risk for inadequate intake of essential nutrients. Inadequate nutrient intake can impact morbidity and mortality in patients with heart disease.

MONITORING

A key element of every nutrition plan is reassessing and modifying as needed to meet the needs of the patient over time. Dogs with cardiac disease can remain stable for many years and may not experience progression of disease. Feeding a complete and balanced diet and maintaining a healthy body condition are important components of managing a dog with heart disease. Although a diet change may not be necessary in early stages of heart disease, discussing dietary strategies early can improve outcomes. Demonstrating to the pet owner how to monitor for changes in respiratory rate and effort as well as changes in lean body mass and body condition can aid the pet owner in determining when they should seek veterinary care for their dog with heart disease.

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COMMON CARDIAC DISEASES OF CATS

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KEY TAKEAWAYS

- Hypertrophic cardiomyopathy is the most common heart disease in the domestic cat. Another cardiovascular condition in cats is systolic hypertension.
- Diet has not specifically been shown to significantly alter therapy for cardiac diseases in cats although newer drugs and treatment may be likely to do so.
- Achieving and maintaining an ideal body condition score in underweight patients and maintaining muscle condition and a consistent appetite are important nutritional goals in cats with cardiovascular diseases.

HYPERTROPHIC CARDIOMYOPATHY (HCM) AND HYPERTROPHIC OBSTRUCTIVE CARDIOMYOPATHY (HOCM)

Overview

Hypertrophic cardiomyopathy (HCM) is the most common form of heart disease in the cat with heritable characteristics. It often progresses over a few years starting with a low intensity systolic murmur, ventricular thickening, and mitral valvular insufficiency. Some cats remain asymptomatic whereas others develop signs that require therapeutic attention.

Cats must be carefully examined for HCM. Other causes for a similar murmur include dehydration, cardio-renal syndrome, coronary arterial disease, aging with systemic hypertension, atrial tachycardia, hyperthyroidism, aortic stenosis, and diabetes mellitus as well as a congenital heart defect in a young kitten. A high prevalence for HCM is observed in purebred cats such as the Sphinx, British ragdoll, and Maine coon; however, because domestic shorthair (DSH) cats are so prevalent in the population, this disease is not breed restricted.

Diagnostics

A soft systolic murmur (2–4/6) characterized as an evenly pitched, soft systolic sound is auscultated between the 3rd to 5th intercostal spaces. As cardiac insufficiency develops, a third heart sound (gallop) may be present in early diastole or a fourth heart sound (gallop) just preceding the first heart sound may be auscultated.

When HCM is not associated with left ventricular (LV) outflow obstruction the echocardiogram (ECHO) identifies thickening of the LV walls and mitral valve regurgitation. An associated cardiac condition that requires differentiation from HCM is hypertrophic obstructive cardiomyopathy (HOCM), which has an additional component observed on the ECHO. That occurs when the anterior leaflet of the mitral valve moves against the LV outflow tract in systole, causing an obstruction to outflow dynamics.

HCM and HOCM usually are identified in young to middle-aged cats but occasionally are seen in both younger and older cats.[1] There are numerous reasons for murmurs to develop in cats with clinical diseases that require differentiation. [2]

The ECHO remains the gold standard for diagnosis of HCM and HOCM. In both cases, there is marked thickening of the left ventricle greater than 0.6 mm, obstruction to blood flow across the aortic valve, and left atrial distention—all causing hemodynamic dysfunction. Right and left heart failure and pulmonary edema develop with signs that include increased resting respiratory rate (RRR), dyspnea, bluish mucous membranes, severe respiratory distress, a drop in systemic arterial blood pressure and, ultimately, cardiac arrest.

When the disease is associated with a left atrial thrombus, if an arterial embolism occurs and causes an obstruction to a major peripheral systemic arterial supply, the patient can decline quickly. There is an

arterial obstruction usually, although not always, at the femoral bifurcation. A loss of blood supply to the affected body part (often renal) results in ischemia and often shock, along with one or both rear limbs becoming pulseless, severely painful, and cold. The obstruction may cause the loss of function in the affected limbs, sudden death, or severe pulmonary edema. In these situations, the owner should be advised of the poor to grave prognosis and the expense of treatment required for recovery. Partial recovery does occasionally occur.

COMMUNICATION TIP

"Providing a complete and balanced diet with high protein and fat and quality ingredients will likely keep the cat well-nourished."

Radiographic evaluation helps to determine the progression of the heart disease. There usually is a clear distinction between normal and abnormal films of the heart and lungs. Abnormalities include left atrial enlargement on the right lateral view as well as on the DV or VD views. Bulging of the atria bilaterally may demonstrate a valentine-shaped heart on the VD view. This is associated with evidence of venous engorgement on the lateral view and congestion, or pulmonary edema is likely to be present along with pulmonary arterial enlargement.

ECHO measurements that are useful for diagnostic purposes include a view of the thoracic cavity (for free fluid), normalized LV end diastolic size (LVIDDn in diastole, 2.5–5.0 mm is normal), left atrial size (8.5–12.5 mm is normal), thickness of the LV free wall (0.5–0.6 mm is equivocal, greater than 0.6 mm in diastole is an indication of LV hypertrophy) and the LA:Ao in the normal cat is < 1.3. **Figure 1** shows differences seen on ECHO between a normal cat and a cat with HCM.

Therapy

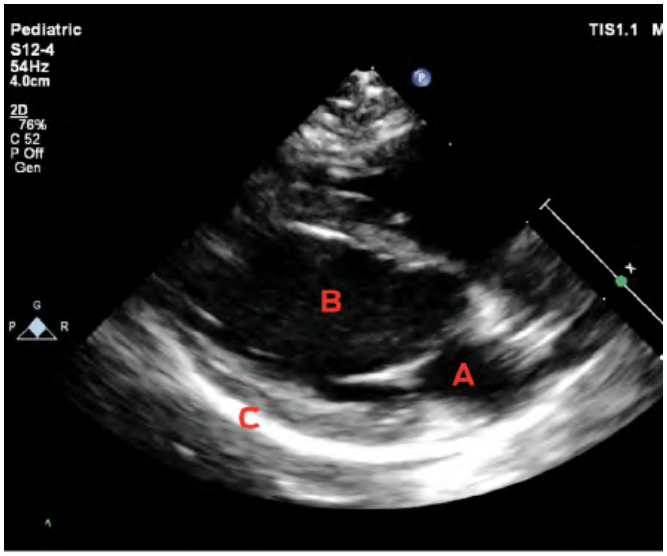
Several drugs were previously thought to be effective in treating cardiomyopathies in the cat. These included beta blocking agents to relax the heart muscle and slow electrical conduction, but they have not been efficacious; nor have calcium channel blocking agents or angiotensin converting enzyme inhibitors (ACEi). We do know that furosemide and torsemide are effective in reducing fluid accumulation. No other singularly administered agent has effectively managed heart failure progression. Fortunately, diuretics are effective but do not slow progression to pulmonary edema and heart failure. Pimobendan has been shown to effectively treat some HCM cats, although it is off-label use. Its use remains controversial. A new class of drugs that acts as a myosin inhibitor has been effective in helping people with this disease and is being studied in cats to determine safety and efficacy.

Dietary Considerations

Experience says that treating non-clinical disease by providing a complete and balanced diet with high protein and fat and quality ingredients will likely keep the cat well-nourished. Body condition should be considered, although one study suggested that cats with average to slightly higher than average body weight have increased survival versus cats that are underweight.[3] Excessive weight loss is a poor prognostic factor. This may be an indication that weight loss was a late sign of the disease's progression. A complete and balanced diet that is palatable to the cat should help to keep the cat eating. We do not know if there is value for dietary salt restriction in a cat with heart failure due to HCM. It is advisable to stop treats that are high in sodium and to keep all treats below 10% of total daily calories. Cats are not creatures of habit and may prefer a varied diet that is high in protein and fat. Restricting a cat's diet to the level of hyporexia or inducing significant weight loss, even when the cat is overweight, is not suggested. Generally, a complete and balanced commercial diet will suffice if palatable and if the cat will eat it routinely.[4] Low-fiber intestinal diets are often good options due to high digestibility, high calorie density, and high palatability. Omega-3 fatty acids (specifically EPA and DHA from fish oil) are beneficial. Diets or supplements that help relax or calm the cat can also be useful when palatable. Hand feeding (usually warmed moist foods) is suggested for hospitalized cases.

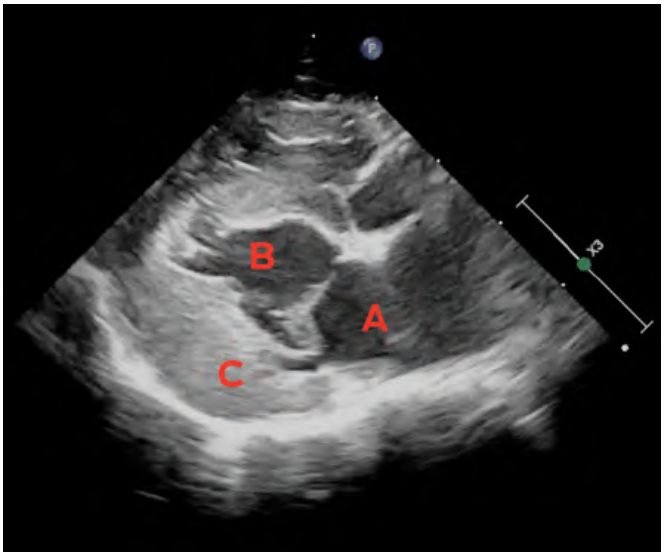
Considering how fussy an adult cat is regarding diet, until we have more specific information and new diets scientifically studied and prepared for cats with known heart disease, a well-balanced diet to keep them eating is our safest approach to early therapy. High-protein

Figure 1. This figure identifies a right lateral echocardiographic image of a normal cat and one with hypertrophic cardiomyopathy (HCM). Note the normal LV cavity and left atrial size in the normal cat compared to the small LV cavity and the thickened LV wall in the HCM cat. ECHO courtesy E. Côté, DVM



A = Left atrium, B = Left ventricular cavity, C = Left ventricular wall

1A. Normal cat's echocardiogram showing a normal LV cavity, small LA and thin LV walls



A = Left atrium, B = Left ventricular cavity, C = Left ventricular wall

1B. Cat with HCM identified by the large LA, thick LV walls and the small LV cavity.

diets may help maintain lean muscle mass and higher fat diets may help ensure adequate intake due to high energy density. Do not send a cat home that is painful or not eating on its own following an embolic episode; only do so if the owner believes that he/she will be able to stimulate the appetite at home. In such cases, expect a likely return to the hospital and possibly a request for euthanasia.

Prognosis

Usually the prognosis once failure has started is guarded to poor, but there is a small percentage of cats that manage these difficulties and do well. Often the long-term prognosis is poor, with death or euthanasia usually occurring within the first several months.

DILATED CARDIOMYOPATHY (DCM)

Overview

Dilated cardiomyopathy is a systolic cardiomyopathy characterized by dilation of the left ventricle and later by all chambers of the heart. The two most common features of dilated cardiomyopathies are marked enlargement of the atria and LV and a marked decrease of contractility. It was considered a primary disease until it was described as a nutritional process associated with decreased dietary taurine levels.[5] Upon supplementation of the amino acid taurine to cooked commercial food, manufacturers have essentially eliminated this disease. It is rarely recognized in practice today. There are occasional cases that present with systolic dysfunction, but these usually do not respond to taurine supplementation.

Diagnosis

Echocardiography confirms the diagnosis of ventricular dilatation, severe atrial enlargement, and hypokinesis (fractional shortening =10–20%). Weight loss, muscle wasting, and anorexia are common, and treatment in the late stage is usually not successful.

Therapy and Dietary Considerations

Early treatment would include the use of diuretics, pimobendan, and digoxin (if atrial fibrillation is present) as well as insertion of a feeding tube until the cat begins to eat on its own. Taurine is administered orally (250 mg twice daily) through the feeding tube. Other drugs such as amlodipine have been suggested but require monitoring.

Getting the cat to eat is a critical part of initial therapy in addition to oral and injectable drugs to sustain

the cat while administering excellent nursing care. Hospitalization where there is 24-hour nursing care is essential. Appetite is less important if a feeding tube has been inserted and medication (ground into powder) can also be administered via the feeding tube until the cat begins to eat on its own. Thereafter, a modestly limited salt diet that is high in energy density, protein, and fat is desirable. Once the cat begins to eat on its own, a complete and balanced diet should be provided. Techniques to help improve food intake in hospitalized patients can be found in the practical tool entitled Assisted Feeding and Using Feeding Tubes in Canine and Feline Practice. Taurine is then added to the food at 250 mg twice daily. Diets should be high protein and high fat, complete and balanced, and highly palatable. Non-meat (vegetarian) diets are not recommended.

Prognosis

DCM has a poor prognosis and taurine, even when supplemented, does not improve the cat's dire potential for recovery. Most cats succumb days to weeks after the diagnosis is made because the condition is so advanced when diagnosed and when treatment is started. Cases seen since the recognition of the cat's taurine requirement usually do not fare well with treatment.

SYSTOLIC HYPERTENSION

Systolic hypertension is a condition that commonly affects older cats and is a primary or secondary cardiac disease. In older cats it is difficult to identify which condition came about first.

Diagnosis

Systolic hypertension infrequently may be recognized by the owner when there is a sudden loss of vision (amaurosis). Indirect ophthalmoscopy of cats with systolic hypertension may identify subtle focal retinal edema, retinal hemorrhagic lesions, and peripheral and retinal vascular changes.[6] Many diseases can also be related to hypertension, including moderate to advanced renal dysfunction (many causes), adrenal gland dysfunction (adrenal medullary changes), and hypertrophic cardiomyopathies.

Systolic pressures are considered high when the pressures exceed 160–180 mmHg. A reading of over 180-200 mmHg is considered elevated in most younger cats or in those that are very anxious. Pressures and heart rate (HR) in kittens are often meaningless.

Box 1. Important nutrients in the management of common heart diseases in cats

- Calories/energy: helps maintain body weight and body condition
- Protein: helps maintain lean muscle mass
- Fat: energy-dense, helps provide more calories in a small volume of food
- Taurine: an essential nutrient in cats; deficiency can cause DCM (but newer cases of DCM in cats appear to be unresponsive to supplemental taurine)
- Sodium: moderate restriction may help manage systemic hypertension in cats, but the evidence is not definitive (nor have any scientific studies identified the appropriate levels)
- Omega-3 fatty acids, EPA and DHA: support cardiac health and reduce inflammation

Pressures recorded in the anxious cat in the veterinary hospital are not to be trusted initially, while those taken after sedation may hide the true pressure. An oft-used technique is to have a veterinary technologist measure the systolic blood pressure in the examination room with the lights dimmed, the owner perhaps assisting or calming the cat after a 10- to 15-minute quiet period before the veterinarian joins the examination (white coat effect). Most blood pressure measurements are made via indirect manometry using a rear leg or the tail artery to obtain a reading. If the cat is quiet and remains so during the recording, these results are likely to be trusted. Pressures in wild, frightened, or just difficult cats (in the exam room, not at home) should be disregarded or adjusted for what is thought to be abnormal. Even better in these situations is to redo the measurements without the owner being present, in a darkened and particularly quiet examination area.

Treatment

In addition to dietary management, there are drugs that effectively lower the heart rate and systolic blood pressure. Included in this group are the beta blocking agents (class 2 anti-arrhythmic drugs), such as propranolol and atenolol, that are discussed in

greater detail in internal medicine treatises.[4] Also effective are some calcium channel blocking agents (class 4 anti-arrhythmic drugs) such as amlodipine and diltiazem. Additionally, antihypertensive agents such as angiotensin converting enzyme inhibitors (ACEi) and angiotensin receptor blocking agents (ARBs) may be considered. A compound recently reported for its positive effect on reducing renal hypertension in cats is telmisartan, an ARB agent. There are many effective protocols for reducing systolic hypertension, although at times the condition appears to be untreatable.

Dietary Considerations

Dietary management of systolic hypertension has not been directly studied in the cat when compared to non-dietary efforts. In humans, lower sodium diets are strongly recommended, but it has yet to be identified if dietary management is useful or not in the cat. It is recommended that high-salt diets and treats be avoided if systemic hypertension is present.[4] Protein and fat help maintain lean muscle mass and increase palatability. Low-salt diets are often very unappetizing for cats, and they may quickly reject them. The diet should be well balanced, with increased high-quality protein and fat provided there are no contraindications to such a diet. Treats should be lower in sodium and kept to no more than 10% of total daily calories.

CONCLUSIONS

Heart disease in cats, even the most common conditions, can be difficult to manage. It is important to perform diagnostics to identify the issue, initiate medical management, and consider nutrition as part of multi-modal therapy. The most important considerations for nutrition are maintaining adequate food intake and monitoring the nutritional assessment to help maintain body weight, body condition score, and muscle condition score as best as possible throughout the course of disease. Key nutrients in the management of heart disease in cats are summarized in **Box 1.**

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PRACTICAL TOOL: GUIDELINES FOR STAGING MYXOMATOUS MITRAL VALVE DISEASE IN DOGS

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Chronic mitral valvular heart disease is the most common heart disease of dogs. It generally occurs in middle-aged to older dogs and is heritable. Not every dog with myxomatous mitral valve disease (MMVD) is significantly affected, and the disease is usually a long-term progressive process. The ACVIM Cardiology Specialty developed a staging system providing a simple, easy to follow set of recommendations regarding its treatment.[1] While not all cases are the same, there are new and older evidence-based studies that separate the different stages of the disease and suggest treatments for each subset (**Table 1**). Whereas the disease is progressive, it is treatable but not curable. Multiple cardiac diseases affect dogs' hearts. This staging applies to MMVD only, although it may be applicable to some cardiomyopathies.

COMMONLY REQUIRED MEDICAL PROCEDURES

The stages are best identified via a complete history and physical examination (PE) that includes body weight and body condition score (BCS), muscle condition score (MCS), mucous membrane color (MM), venous return, tracheal palpation at the thoracic inlet, careful auscultation of the heart in all four valve regions, and lung sounds. When present, abnormal cardiac signs include a short systolic murmur that increases in intensity and duration over time as MMVD progresses. The murmur is best heard over the left 4th to 6th intercostal space, initially as a soft, early systolic sound. Depending on the presence of clinical signs, no additional testing may be required, or a full examination may be recommended.

Other testing that is usually completed as part of a full cardiac examination includes thoracic radiographs (two view with small portions of the cranial and caudal lung parenchyma viewable). These are indispensable for documenting cardiac chamber size and total heart size utilizing one of several techniques that define cardiac remodeling (vertebral left atrial size [VLAS] > 3 vertebrae; vertebral heart score [VHS] > 11.5 vertebrae). There are significant breed variations that make these numbers often unreliable.

Laboratory tests can evaluate other organ dysfunction and measuring serum NT-proBNP (N-terminal pro B-type natriuretic peptide) and cardiac (HS [high-sensitivity]) troponins is considered appropriate in dogs with cardiomegaly. Depending on the severity of the signs, an echocardiogram (ECHO) helps to identify early through late stages of cardiac remodeling. ECHO numbers suffice to provide the information required to make an accurate assessment of MMVD status.

To avoid a cookie-cutter approach we have adopted a system that allows an accurate description of each category. No doubt over time this, too, will be updated, but for now it presents a very realistic way for you, the practitioner, to separate the clinical phases confidently. Follow the next few paragraphs to see how using clinical signs and easy steps in your clinic will separate the stages of MMVD disease.

STAGING OF MMVD (FIGURE 1)

Stage A: At Risk

Noted in most small breeds of dogs that are predisposed genetically, these dogs have no murmur or clinical signs and do not require medication or a special diet. They should be examined on an annual basis (or more frequently) and a murmur, if present, should be described in the medical record.

Stage B1: Preclinical Disease

Preclinical disease may be present in dogs at an early stage or later in life.There are no clinical signs, and only a short, soft systolic murmur may be present upon auscultation. Mild cardiomegaly may be noted radiographically or upon review of an echocardiogram. The resting respiratory rate (RRR) remains normal. Early signs of remodeling rarely are present, and the ECHO measurements are usually normal.

Table 1. Guidelines to therapy for dogs with MMVD

Stage	Clinical Signs	Radiographs	Echocardiogram	Medications	Prognosis	Diet
Stage A: genetic, historical, at risk	None Normal dog	Normal	Normal No mitral regurgitation	No	Good	No changes needed
Stage B1: early; mild	Potential soft murmur	Normal	Normal Mild mitral regurgitation (+)	No	Good	Dietary modification may not be needed for cardiac disease, may be needed for other problems
Stage B2: moderate	Increased systolic murmur? 2-4/6 Increased RRR? Increased cough? Nocturnal cough?	Early enlarged heart size; increased VHS Slightly increased LVE? No pulmonary edema or venous congestion	La:Ao N=< 1.6 LVIDDn N=< 1.7 Mitral regurgitation (++) Fractional shortening slightly increased	Yes – oral medication Pimobendan or Benazepril and Spironolactone Antitussive (hydrocodone) as needed	Guarded	Dietary modification recommended Limit sodium High quality protein Highly digestible Supplement omega-3 fatty acids EPA and DHA Ensure adequate energy/calorie intake
Stage C: advanced	Grade 4–6/6 systolic murmur and gallop sound is likely present Dyspnea & increased RRR Cough – frequent/ harsh Venous distension +/- Pulmonary edema +/-	Left atrial enlargement (+++) Left ventricular enlargement (+++) No to mild venous distension VHS enlargement (+++)	Left atrial enlargement (+++) Left ventricular enlargement (+++) LVIDDn > 1.7 Mitral regurgitation (+++) Venous engorgement Fractional shortening (+++) Potential arrhythmia	Yes – oral &/or subcutaneous Pimobendan or ACE inhibitor + Spironolactone Furosemide and/or Torsemide (oral; SC; IV)	Short term limited Long term poor	Dietary modification needed Restrict sodium High quality protein Highly digestible Energy dense diet Supplement omega-3 fatty acids EPA and DHA Potential therapeutic cardiac diet or complete and balanced home-cooked diet Ensure adequate energy/calorie intake

Table 1. Guidelines to therapy for dogs with MMVD *continued*

Stage	Clinical Signs	Radiographs	Echocardiogram	Medications	Prognosis	Diet
Stage D: severe	Advanced congestive heart failure Increased heart rate Pulmonary edema Marked respiratory distress Muddy mucous membranes Likely arrhythmia (supraventricular &/or ventricular premature beats; atrial fibrillation)	Left atrial enlargement (+++) Left ventricular enlargement (+++) Pulmonary venous enlargement Pulmonary edema likely present VHS (++++)	Same as Stage C with severe left atrial enlargement Potential arrhythmias Same as Stage C but more advanced	All drugs mentioned for Stage C with variable dosage increases Digoxin Calcium channel blockers – Amlodipine IV milrinone, dopamine or other inotropes or pressors Hydralazine orally in emergency edema	Poor to grave	Same as Stage C Offer warmed food and use other tactics to increase food intake as needed

ACEi = angiotensin converting enzyme inhibitor; DHA = docosahexaenoic acid; EPA = eicosapentaenoic acid; La:Ao = left atrial to aorta size ratio; LAE = left atrial enlargement; LVE = left ventricular enlargement; LVIDDn = left ventricular internal diameter normalized; RRR = resting respiratory rate; VHS = vertebral heart score

Modified and updated with additional information provided by the cited references and by the author

Treatment of stage B1 dogs: No medications are necessary for this stage of disease, and dietary modification may be beneficial in some cases, especially if concurrent disease is present such as obesity or gastrointestinal disease. Rechecks should be annually or more frequently.

Stage B2: Moderate Heart Disease

The murmur progresses, and cardiac remodeling is recognized radiographically or on the ECHO.

At this stage of disease there is progression from being without clinical signs to a stage that suggests left atrial enlargement (LAE) and potentially early retention of fluid (venous stasis). Some of these patients may be vacillating in and out of early heart failure. Some clinical signs develop leading the caretaker to complain of signs such as a nocturnal cough, restlessness, exercise intolerance, and/or an increase in the RRR. The heart murmur has usually increased to a 3–4+/6 holosystolic; lung rales may or may not be present; and the ECHO is consistent with early cardiac remodeling (particularly, LA:Ao enlargement beyond 1.6 and an increase in LV diameter normalized in diastole [right side 4 chamber view] exceeding LVIDDn > 1.7). If echocardiography is not available, an increase of either the VLAS > 3 or VHS > 11.5 is likely observed radiographically.

Treatment of stage B2 dogs: Several approaches to treatment of B2 dogs are available. One route encourages starting pimobendan orally.[2] An ACE inhibitor (ACEi) (Benazepril/Enalapril) plus spironolactone may also be beneficial for these patients.[3] The difference between stage B2 and C is not linear and is often unclear. Limited exercise, home therapy, and diet with a modest salt intake is suggested. Omega-3 and -6 fatty acids supplement the diet; high quality protein and high digestibility are suggested. Rechecks are advised every 3–6 months (as required), and signs of increased RRR hint at progression of cardiac dysfunction. Failure to respond identifies the need for re-evaluation of the diagnosis and/or changing drug therapy. Anti-tussive agents may be needed as adjunctive therapy.

Stage C: Moderate Heart Failure

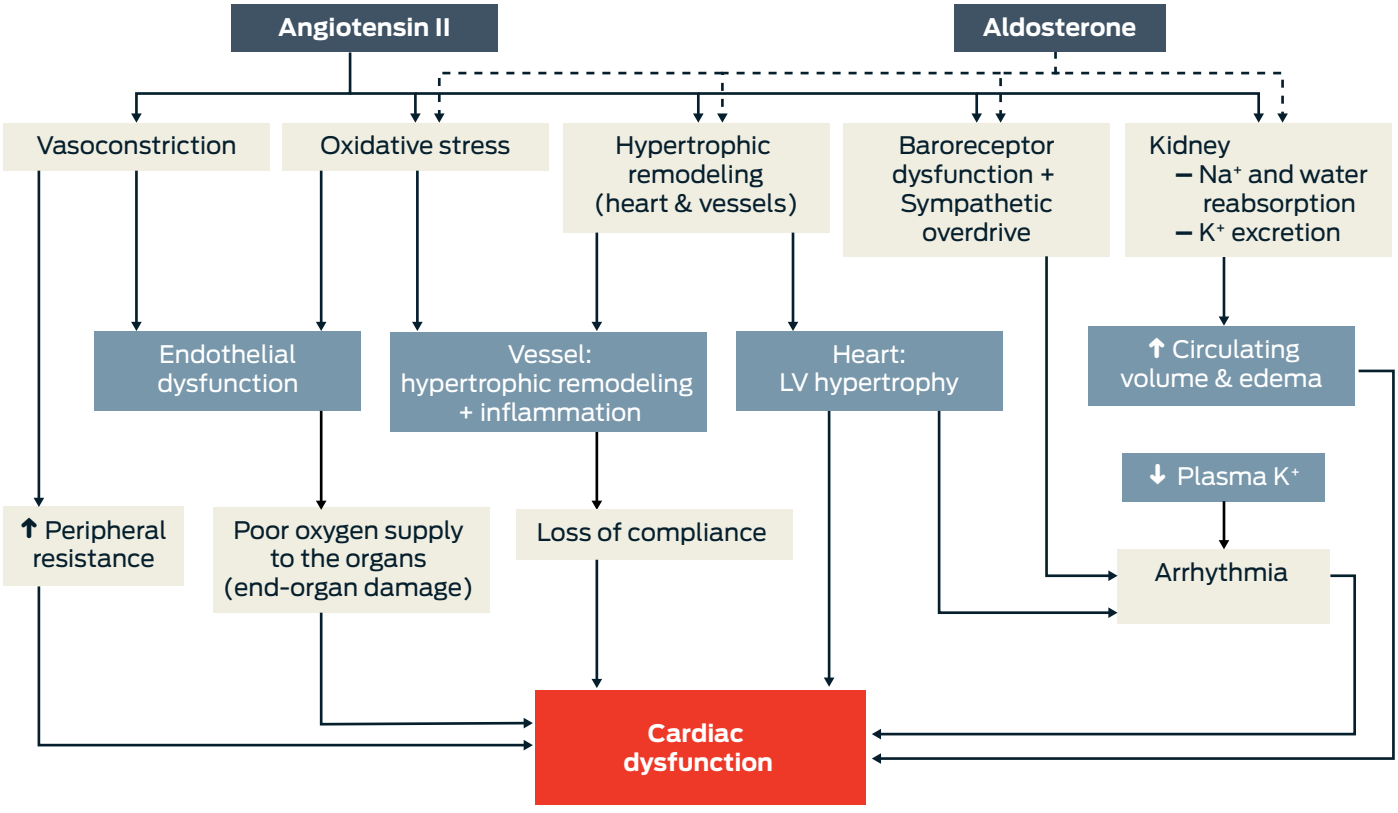
This stage, with moderate to severe fluid accumulation, indicates moderate heart failure.

Since the progression of B2 to C is never perfectly clear, this stage marks the transition from a heart that is slightly malfunctioning to one that is significantly affected. It shows marked cardiac remodeling due to disease progression. All the above-mentioned criteria for heart failure are present although in some cases, the dog does very well for variable periods of time utilizing oral and/or injectable therapies.

A brief period in a cooled and humidified O2 cage helps to reverse acute respiratory distress. The most significant clinical signs are an increase in the RRR, nocturnal and/or daytime coughing, and intolerance to moderate or strenuous activity; syncope may accompany this stage.

Treatment of stage C dogs: Oral pimobendan or an ACEi plus spironolactone (**Figure 1**) is suggested along with the addition of a diuretic to reduce fluid retention. Diuretics given one or more times daily should rapidly result in extracellular fluid control (i.e., increased urine production) and clinical improvement. Restricted sodium intake is helpful but should not be excessive as diet palatability is significantly reduced. Supplementing the diet with omega-3 and -6 fatty acids and an energy dense complete and balanced home-cooked diet or a commercially available diet with modest sodium restriction may help; these should contain good quality protein and be highly digestible. Patients may develop anorexia/hyporexia and/or cachexia, so it is important to monitor appetite, body condition score (BCS), and muscle condition score (MCS). Pet treats are not suggested due to their excessive sodium and calorie content. Exercise restriction is strongly recommended; however, most pets at this stage will likely self-limit. Butorphanol to limit coughing and excitement may be necessary. Other conditions to consider, especially when there is limited or no progress, include irregular cardiac rhythms, rupture of a chordae tendineae or a papillary muscle, partial tear of the atrium, significant electrolyte disturbances, pericardial effusions, renal dysfunction, systemic and/or pulmonary hypertension, and abdominal and/or thoracic effusions. Failure to respond to one of the two inotropic "type" drugs, injectable and/or oral diuretics (furosemide or torsemide), and sodium and exercise restriction is an indication that another problem may have developed and should be scrupulously searched for. Centesis of abdominal or thoracic effusions may be required. Additional testing is suggested such as physical examination, EKG, serum biomarkers and chemistries, CBC, and repeat thoracic films. Monitoring for electrolyte disturbances and renal dysfunction

Figure 2. Deleterious effects of Angiotensin II and Aldosterone in dogs with MMVD



is necessary as visits to the hospital become more frequent.

Stage D: Overt Congestive Heart Failure

This near terminal state may be an indication of advanced progressive disease or poorly controlled pharmacologic therapy. The dog experiences marked respiratory distress, may be cyanotic, and expresses severe weakness, dyspnea, an extended neck, and open mouth breathing, all of which are associated with pulmonary edema. A rapid (and irregular [atrial fibrillation]) cardiac rhythm, rapid or slow arrhythmias, and other signs of progressive heart failure including cavitary effusions may be present.

Treatment of stage D dogs: Treatment must be aggressive and thorough. Hospitalization is strongly recommended at a fully staffed 24-hour facility where specific attention can be provided to the pet. Basic testing may need to be limited until breathing is normalized. Mild sedation (IV butorphanol or buprenorphine) is a requisite for the distressed and frightened pet. Cage rest is essential. Drug therapy as previously discussed is required; however, in addition to the recommended oral and injectable products, additional or increased diuretics may be needed (2–3x daily). Handling of the dog should be avoided until the pet is better stabilized. As last attempts are made at salvage, infusions of IV pimobendan, milrinone, or dopamine may be considered. As severe as these signs are, occasionally a dog responds well and goes on to continue comfortable living.

Note to reader: *There are many products that have been recommended for the treatment of advanced heart failure. Many have been shown to be ineffective, particularly those that are nutraceuticals or herbal in nature. Others may include varying diets, untested drugs, and appetite stimulants. While a few may have a short-term beneficial effect, many have little to none. If the client wishes to pursue care with any of these products, note this in the record and identify that they are being used with limited veterinary recommendation and are being utilized following a client's request when other modalities of therapy have been exhausted. Clients are likely to request supplements for their pet. Explain to them that the dog is already receiving multiple medications and adding more is likely only to cause further anorexia and cachexia.*

A final notation reinforces the discussion regarding quality end-of-life care. Some clients will choose to extend life, not realizing the level of discomfort being experienced by their pet. Gentle but firm discussions are due at that point. Quality of life is a significant factor in trying to provide for end-of-life care. Direct but gentle discussions are required, and thorough notes in the record are essential when the client denies the outcome of prior discussions. ***This is when the art of practice meets the art of compassion and communication.***

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CRITICAL CARE

CRITICAL CARE NUTRITION IN DOGS AND CATS

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KEY TAKEAWAYS

- A nutritional support plan should be integrated in the treatment plan for all critically ill patients
- Setting appropriate calorie targets that avoid overfeeding but are sufficient to meet presumed needs may be crucial in reducing patient morbidity and may positively impact patient outcomes
- With proper patient selection, sound nutritional planning, and careful monitoring, nutritional support may play an important role in the successful recovery of many critically ill patients

INTRODUCTION

Nutritional support is now considered an essential part of managing critically ill patients, especially if they are malnourished. Although there is convincing evidence of the deleterious effects of malnutrition in people,[1] the optimal nutritional strategies for critically ill animals still require further investigation.[2] What is known is that the risk of malnutrition in this patient population often relates to insufficient food intake and catabolic effects relating to underlying disease conditions and concurrent morbidities. Because malnutrition can occur quickly in these animals, it is vital that we identify animals at risk for malnutrition and initiate early nutritional support for these patients. The goals of nutritional support are to manage malnutrition when present and to prevent malnutrition from developing in these patients.

Whenever possible, the enteral route should be used because it is the safest, most convenient, and most physiologically sound method of nutritional support. Ensuring the successful nutritional management of critically ill patients involves selecting the right patient, making an appropriate nutritional assessment, and implementing a feasible and effective nutritional plan.

THE IMPORTANCE OF NUTRITIONAL SUPPORT

The metabolic responses to injury and illness are complex and place critically ill animals at high risk for malnutrition and its deleterious effects.[1,3] These effects include altered energy and substrate metabolism, compromised immune function, and impaired wound healing.[1,3] Many of the challenges encountered when managing critically ill patients relate to the presence of organ dysfunction (e.g., ileus, diarrhea, azotemia), gastrointestinal intolerance (e.g., nausea, regurgitation, vomiting), metabolic complications (e.g., acidosis, hyperglycemia, hypokalemia) and the presence of comorbidities (e.g., weakness, significant weight loss, kidney failure) all of which can be barriers for effective feeding (**Box 1**). Lack of enteral nutrition will further contribute to abnormal gastrointestinal function such as the development of ileus and loss of mucosal barrier function.[2] There is now some evidence that with early nutritional support, animals can have improved outcomes.[4,5] Therefore, it is vital that clinicians managing critically ill patients explore ways of initiating early nutritional support whenever possible.

CONSEQUENCES OF MALNUTRITION

One of the major metabolic alterations associated with critical illness involves body protein catabolism, in which protein turnover rates may become markedly increased.[3,6-8] Whereas healthy animals primarily lose fat when temporarily deprived of sufficient calories (i.e., 'simple starvation') as may be encountered by fasting animals before surgery, sick or traumatized patients catabolize lean body mass when they are not provided with sufficient calories (i.e., 'stressed starvation'). In this catabolic state, lack of sufficient food intake leads to glycogen stores being depleted, especially in strict carnivores such as the cat, and this leads to an early mobilization of amino acids from muscle stores.[9,10]

Box 1. Barriers to effective food intake in dogs and cats

- Pain
- Vomiting
- Regurgitation
- Nausea
- Ileus
- Mental depression/stupor
- Weakness
- Pyrexia

As cats undergo continuous gluconeogenesis, the mobilization of amino acids from muscles is more pronounced than that observed in other species.[9,10] With continued lack of food intake, the predominant energy source is from accelerated proteolysis (muscle breakdown), which in itself, is an energy-consuming process. Muscle catabolism that occurs during stress provides the liver with gluconeogenic precursors and other amino acids for glucose and acute-phase protein production. The resultant negative nitrogen balance or net protein loss has been documented in critically ill dogs and cats.[7]

The consequences of continued lean body mass losses include negative effects on wound healing, immune function, strength (both skeletal and respiratory muscle strength), and ultimately on overall prognosis. In dogs, a period as short as 3 days of anorexia has been documented to produce metabolic changes consistent with those seen associated with starvation in people.[11] However, these dogs would not necessarily exhibit any easily detectable abnormalities on clinical assessment suggestive of being malnourished. Dogs with overt signs suggestive of malnutrition (e.g., severe muscle wasting, poor coat quality) (**Figure 1**) usually have a more protracted period (usually weeks to months) of disease progression. Detectable impairment of immune function can be demonstrated in healthy cats subjected to acute starvation by day 4, and recommendations to institute some form of nutritional support in any ill cat with inadequate food intake for more than 3 days have been made.[12,13] In both dogs and cats, there is some consensus that there is an urgent need to implement a nutritional intervention (e.g., place feeding tube) when a dog or cat has not eaten for more than 5 days.[14]

A major goal of nutritional support is to minimize metabolic derangements and catabolism of lean body tissues. During hospitalization, repletion of normal body weight is not the top priority because regaining body weight is best achieved once the animal has recovered from the underlying condition. Therefore, there is little justification to feed excessive amounts of calories to critically ill patients.

NUTRITIONAL SUPPORT PLANNING

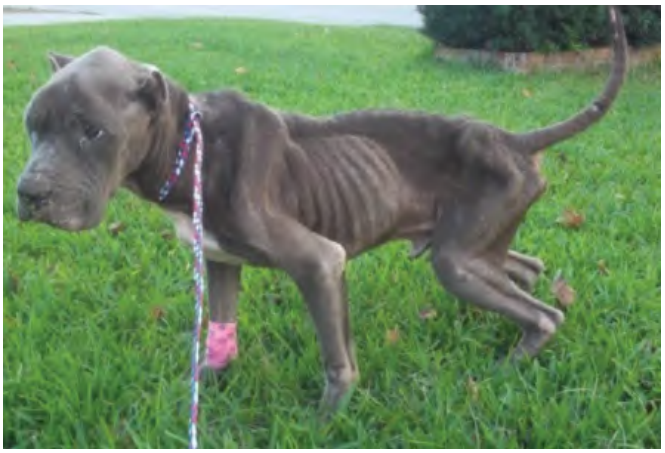
As all nutritional support techniques carry some risk for complications, appropriate nutritional assessment is key to reaping the benefits nutritional support can offer. The process of nutritional assessment involves readily available historical and physical parameters to identify already malnourished patients and those who are at increased risk for complications who will presumably benefit from nutritional interventions. Nutritional assessment is covered in more detail elsewhere and the reader is advised to familiarize themselves with this important process. In short, patient factors found in the patient's history and physical exam findings can be used to categorize the patient as well nourished, suffering from various degrees of malnutrition, or at risk of becoming malnourished, and the nutritional plan is designed to consider and account for these factors.

In managing critically ill patients one important step is to determine whether or not the patient's voluntary food intake is sufficient. For nutritional planning, one must have a caloric goal in mind for the patient, select an appropriate food, and formulate a feeding plan that is well documented in the hospital treatment instructions. This will permit an accurate accounting of how much food is offered to the patient and will allow evaluation of the patient's intake based on how much of the food is consumed.

CHOOSING THE ROUTE AND FORM OF NUTRITIONAL SUPPORT

Determination of the route of nutritional support (broadly categorized as enteral or parenteral) is an important step in the nutritional management of critical care patients. Enteral nutritional support includes the use of nasoesophageal, nasogastric, esophageal, gastric, and jejunal feeding tubes, while parenteral routes include the use of peripheral and central venous catheters. The route selected for each patient will be

Figure 1. Patients with overt signs of malnutrition, such as the dog depicted in this picture, have significant and prolonged deprivation of calories and nutrients



ultimately influenced by the patient's medical and nutritional status, the anticipated length of required nutritional support, capabilities of the practice, client preferences, financial constraints, and consideration of the advantages and disadvantages presented by each route.

Providing nutrition via a functional digestive system is the preferred route of feeding, and so particular care should be taken to evaluate whether the patient can tolerate enteral feedings. Even if the patient can tolerate only small amounts of enteral nutrition, this route of feeding should be pursued. More focused discussion on the selection and use of feeding tubes is discussed elsewhere (see Practical Tool: Assisted Feeding and Using Feeding Tubes in Canine and Feline Practice). Supplementation with parenteral nutrition should only be pursued when the use of enteral nutrition cannot meet at least 50% of the patient's nutritional needs.

NUTRITIONAL NEEDS OF CRITICALLY ILL PATIENTS

Although nutritional support is recognized as important in the management of critically ill patients, there is much that remains incompletely understood regarding the specific nutritional requirements of critically ill animals. Currently, there are assumptions that nutritional requirements in animals are similar to that of people afflicted with similar diseases. However, it is important to recognize that there may be significant species and disease differences that make such direct comparisons or extrapolations less applicable.

One common goal across species is for nutritional support to optimize or promote protein synthesis and preserve lean body mass.[2] The current recommendation for critically ill animals is to feed at least 5–6 g protein per 100 kcal (25–35% of total energy) in dogs and at least 6–8 g protein per 100 kcal (30–40% of total energy) in cats. Patients with protein intolerance, e.g., hepatic encephalopathy or severe azotemia, should receive reduced amounts of protein (e.g., 3–4 g protein per 100 kcal).[14] When reviewing the subject of critical care nutrition, there is often mention of supplementation of antioxidants, omega-3 fatty acids, and specific amino acids such as arginine and glutamine.[6] While there are some positive results when these nutrients are fed to critically ill people, there is very limited evidence in animals. Nevertheless, these nutrients are often included in critical care diets.

DIET OPTIONS FOR CRITICALLY ILL DOGS AND CATS

The guiding principle regarding diets to be used to support a patient should reflect the nutritional needs of the patient (e.g., higher protein requirements in catabolic patients, fat restriction in hyperlipidemic patients). Generally speaking, critically ill patients should be fed a highly digestible, calorically dense, high protein and fat diet.[14] However, patients that have specific contraindications to high protein (e.g., chronic kidney failure, hepatic encephalopathy) should be fed a moderately restricted protein diet. In animals with gastrointestinal diseases or hyperlipidemia, there may be a need to restrict fat content in the diet. The chosen diet must also be able to be delivered via feeding tubes. Completely liquid diets have the advantage that they can be delivered via any feeding tube. However, many other diets formulated for critical care patients are canned but not in complete liquid form and often require blenderizing the product with water or liquid diet to enable feeding via tubes. In such circumstances, it is important to consider the caloric density of the modified diet as the addition of water will dilute calories.

CALCULATING ENERGY REQUIREMENTS

The patient's resting energy requirement (RER) is the number of calories required for maintaining

homeostasis while the animal rests quietly. The RER is calculated using the following formula:

$$\text{RER} = 70 \times (\text{body weight in kg})^{0.75}$$

Currently, the RER is used as an initial estimate of a critically ill patient's energy requirements, and is achieved gradually over a period of 2–4 days in most critically ill patients.[13] In the context of estimating energy needs of hospitalized critically ill patients, the current weight of the animal, rather than an ideal weight in the healthy state, should be used. It should also be emphasized that these general guidelines should be used as starting points, and animals receiving nutritional support should be closely monitored for tolerance of nutritional interventions. Continual decline in body weight or body condition should prompt the clinician to reassess and perhaps modify the nutritional plan (e.g., increasing the number of calories provided by 25%).

IMPLEMENTING THE NUTRITIONAL PLAN

Regardless of the severity of malnutrition, one must remember that the immediate goals of therapy in any critically ill patient should focus on proper cardiovascular resuscitation, stabilization of vital signs, and identification of primary disease process. The need to follow this general approach stems from the risk of triggering refeeding syndrome, which is rare but a potentially life-threatening condition.[15] Refeeding syndrome is thought to occur when a patient (particularly cats) with prolonged starvation is fed more nutrients than their bodies can assimilate.[15] For this reason, a more conservative approach to initiation of feeding is recommended. As steps are taken to address the primary disease, formulation of a nutritional plan should aim to mitigate overt nutritional deficiencies and imbalances. By providing adequate energy substrates, protein, essential fatty acids, and micronutrients, the body can support wound healing, immune function, and tissue repair.

COMMUNICATION TIP

"Because malnutrition can occur quickly in these animals, it is vital that we identify animals at risk for malnutrition and initiate early nutritional support for these patients."

MONITORING AND REASSESSMENT

Body weights should be monitored daily in all patients receiving nutritional support. However, the clinician should take into account fluid shifts in evaluating changes in body weight. For this reason, body condition score assessment is important as well. The use of the RER as the patient's caloric requirement is merely a starting point. The number of calories provided may need to be increased to keep up with the patient's changing needs. In patients unable to tolerate the prescribed amounts, the clinician should consider reducing amounts of enteral feedings and supplementing the nutritional plan with some form of parenteral nutrition.

With continual reassessment, the clinician can determine when to transition the patient from assisted feeding to voluntary consumption of food. The discontinuation of assisted feeding should only begin when the patient can consume approximately 75% of its RER without much assistance.

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PRACTICAL TOOL: ASSISTED FEEDING AND USING FEEDING TUBES IN CANINE AND FELINE PRACTICE

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Nutritional intervention is critical in the management of hospitalized patients and early enteral nutrition has been directly linked to positive outcomes in human and veterinary patients.[1-5] Veterinary professionals should provide assisted nutrition to animals who fail strategies to encourage voluntary food intake (**Table 1**) and remain hyporexic (eating less than 80% of their resting energy requirement or RER) or anorexic during their hospitalization. Assisted nutrition should be considered for any patient with 72 hours of hyporexia or anorexia.

Feeding tubes are primarily utilized for assisted nutrition in dogs and cats.[6] Feeding tubes are easy to place, can be used short term or long term (depending on the type of tube used), and allow the veterinary professional to easily provide nutrition and oral medications to animals not readily eating on their own. Complications are usually mild, easily managed, and do not preclude the use of the tube when they occur.[7-9] In a recent study, return to appetite occurred in a large population of cats where feeding tubes were utilized, and enteral feeding was also associated with survival in that study.[7] **Table 2** highlights the different types of feeding tubes available to veterinarians and considerations for utilizing them.

When feeding tubes are placed in hospitalized patients, nutritional supplementation should be initiated at 25–50% of the patient's RER (or less) and slowly increased until full RER is obtained. The RER is calculated as $70 \times BW_{kg}^{0.75}$. A clinician can take longer than four days to reach 100% of RER if complications are seen during or associated with feeding. Feedings should be administered at room temperature and slowly to ensure the patient tolerates it. Hands-on feeding demonstration as well as specific feeding instructions should also be provided to the client at the time of discharge.

Table 1. Strategies to increase voluntary food intake in the hospital[6]

1. Treat underlying cause of anorexia (likely most important and most helpful strategy)
2. Treat for nausea (maropitant, metoclopramide as a constant rate infusion, ondansetron)
3. Evaluate patient's medications and consider discontinuing drugs, if reasonable, that may be bitter or associated with inappetence (metronidazole, gabapentin, fluoxetine, opioids, etc.)
4. Provide analgesia in patients who are painful
5. Treat gastrointestinal dysmotility with metoclopramide, erythromycin, or cisapride
6. Provide room temperature food or warm it up for a few seconds in the microwave to release aroma
7. Offer many opportunities to eat regularly—provide a small amount of fresh food every 4-6 hours. Avoid insisting on a prescribed diet when hospitalized and allow patient to eat whatever they prefer to eat
8. Remove uneaten food within about 20-30 minutes of offering the food to the patient to prevent food aversion
9. Feed in quiet places with minimal interruptions (e.g., an exam room). This is especially important in cats
10. Hand feeding, especially for dogs
11. Feed with the owners present, provide familiar food and/or bowls if possible
12. Create positive associations with food when possible (and avoid negative ones)
13. Utilize appetite stimulants (capromorelin orally, mirtazapine orally or transdermally)

Table 2. Common feeding tube types and considerations[6]

Feeding Tube Type	Duration of Use	General Anesthesia Required	Diet Type Required	Advantages	Disadvantages	Contraindications
Nasoenteric tubes nasoesophageal, nasogastric (NE and NG)	Short term (3-7 days)	No, mild sedation only	Liquid enteral diet	Inexpensive. Quick and easy to place. Can be used immediately. Tube of choice for most critically ill patients	May be prone to obstruction. Non-liquid medications may also obstruct the tube. Primarily used in the hospital. Small bore tube, necessitating a liquid diet.	Nasal disease or trauma, central nervous disease with concern for elevated intracranial pressure (e.g., traumatic brain injury), animals with profound obtundation or a poor gag reflex, coagulopathy
Esophageal tube (E-tube)	Long term (weeks to months)	Yes	Liquid enteral diet, canned food slurry	Inexpensive. Quick and easy to place. Many dietary options for use with tube, well tolerated. Can be used immediately and removed anytime. Easy to administer liquid and non-liquid medications. Can be used at home. Tube of choice for patients who need longer term nutritional support (hepatic lipidosis, jaw fractures, pancreatitis)	Requires general anesthesia. Stoma site infection is not uncommon. Can become obstructed.	Animals at high risk for general anesthesia, esophageal disease
Gastrostomy tubes: surgically or percutaneously placed (PEG)	Long term (weeks to months)	Yes	Liquid enteral diet, canned food slurry	Large tube that allows for many dietary options. Suitable for use at home. Easy to administer non-liquid medications.	Requires surgical or endoscopy placement with special training. Risk for peritonitis and stoma site infections. May not be used immediately (PEG) and, depending on tube type and technique, may not be removed for 10-14 days[10]	Animals at high risk for general anesthesia, diffuse and profound gastric disease (neoplasia, severe gastritis)
Jejunostomy tubes	Short term (3-7 days)	Yes	Liquid enteral diet	Bypasses stomach and pancreas which may be helpful in some diseases (severe pancreatitis)	May not be used immediately depending on placement technique.[9,11] Early removal (before day 5) may have serious consequences. Risk for stoma site infection and peritonitis. Not suitable for use at home. Requires special training for placement. Small bore tube, necessitating a liquid diet	Animals at high risk for general anesthesia, animals with peritonitis

Note that there are other less commonly utilized feeding tubes (gastrostomy-jejunostomy, pharyngostomy tubes) that are not included in this list.

Figure 1. A properly placed nasogastric tube. Note that the tube is dorsal to the larynx and in the esophagus (red circle) in the neck. The tube terminates in the stomach (yellow circle). Although the tube deviates ventrally in the mid-thorax (blue circle), there is no question this tube is in the esophagus as confirmed by the dorsal position relative to the larynx (red circle). Image source: Adesola Odunayo

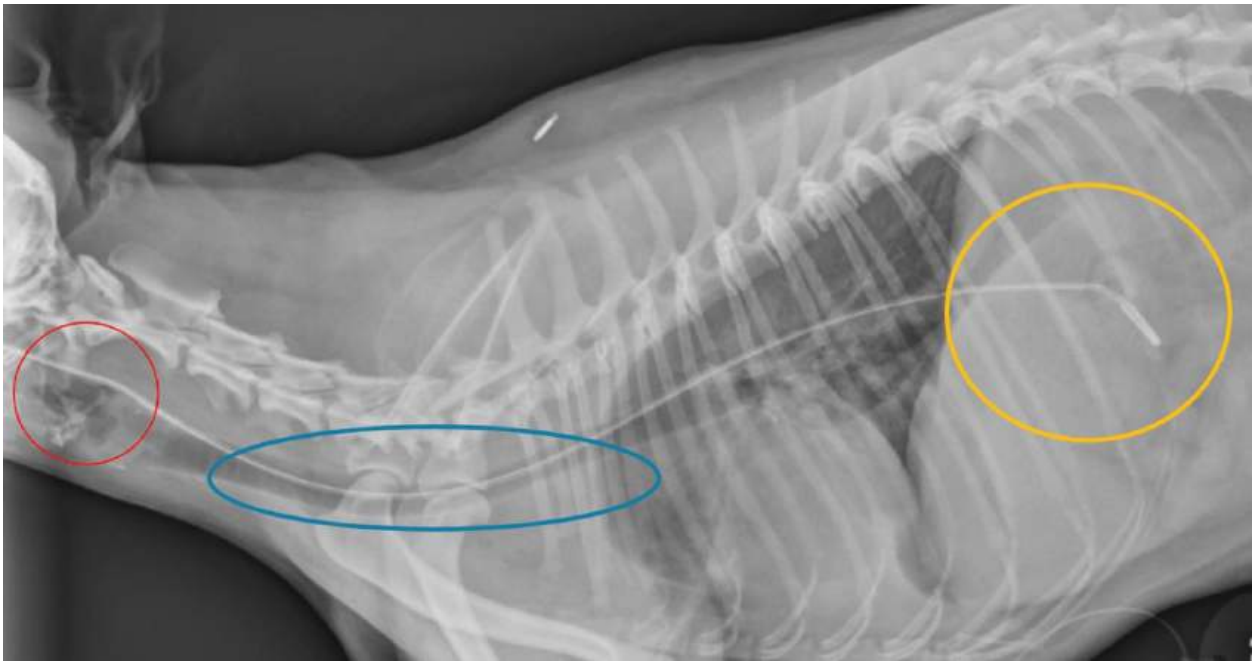
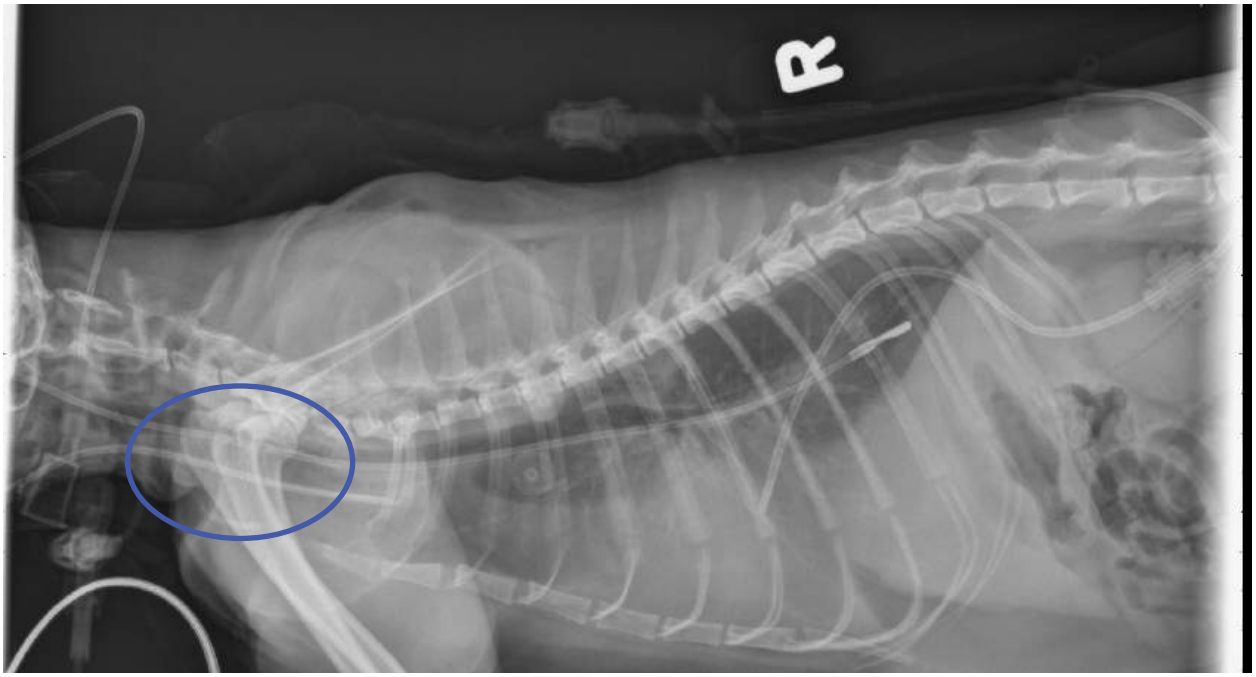


Figure 2. Wrongly placed nasoesophageal tube. Tube (blue circle) is located in the trachea. Image source: Adesola Odunayo



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PURINA Institute

Advancing Science for Pet Health

DERMATOLOGIC DISEASE

ADVERSE FOOD REACTIONS IN DOGS AND CATS

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KEY TAKEAWAYS

- Cutaneous adverse food reactions are not clinically distinguishable from canine atopic dermatitis or feline atopic syndrome and require a dedicated food elimination trial for correct identification and diagnosis.
- Other currently available diagnostics, including serological, intradermal, patch, hair, and saliva testing, are not reliable and are not recommended.
- Client education and communication are fundamental in every part of the diagnostic process. There are several dietary options for a food elimination trial: adjusting to the client and patient's needs will increase the chances of a good outcome.

OVERVIEW

The most common causes for owners to seek veterinary care for their pets are gastrointestinal and skin problems.[1] Adverse food reactions can provoke pruritic behaviors and skin changes and may cause gastrointestinal disturbances in dogs and cats.[2] The veterinary team should be able to identify patients that could be having adverse food reactions and recommend a diagnostic food elimination trial to diagnose and treat such patients.

A careful and detailed clinical history, including a diet history, is key for any veterinary consultation and even more so for dermatological patients. Small details help determine the course of the diagnostic process and the patient's needs. More recently, dermatologists and gastroenterologists have taken notice of patients that present with complaints related to both skin and gastrointestinal problems. These can only be recognized if the right questions are asked. Our dermatology practice includes a gastrointestinal questionnaire that helps us detect patients with GI problems, which some owners may consider normal or irrelevant to the presenting complaint. Asking about dermatological signs in patients with chronic gastrointestinal problems may also be important. A pruritus scale will help determine the level of itch in every patient at the initial consult and on follow-up visits; a cat-specific pruritus scale should be used for feline patients.[3,4]

Adverse food reactions can manifest in different ways in feline and canine patients (**Table 1**). Recently, the classification for allergic disease in the cat has been revised.[5] Adverse food reactions or feline food allergy is considered part of the Feline Atopic Syndrome (FAS). Cats with adverse food reactions can present different skin reaction patterns: head and neck pruritus, self-induced alopecia, miliary dermatitis, eosinophilic granuloma complex, and other skin manifestations such as urticaria, non-pruritic nodules, or plasma cell pododermatitis.[5] Gastrointestinal signs may include vomiting, diarrhea, weight loss, and poor appetite.[6,7] Feline atopic skin syndrome is caused by environmental allergens but cannot be distinguished clinically from adverse food reactions with cutaneous presentations.

Cutaneous adverse food reactions in dogs manifest primarily as non-seasonal pruritus: licking, chewing, and rubbing are common behaviors in itchy dogs, as well as secondary skin infections and chronic secondary lesions. Infections will also contribute to the itch and inflammation cycle.[7] Angioedema and urticaria can also be associated with adverse food reactions, and other less frequent manifestations have been documented, including erythema multiforme, onychodystrophy, perianal fistula, and vasculitis.[8-12] Acute, recurrent, or chronic otitis can commonly present in these patients.[2,13,14] Other non-cutaneous manifestations include respiratory and gastrointestinal disturbances, such as chronic diarrhea, vomiting, borborygmi, increased bowel movements, belching, or gas.[2,13] Clinical signs are summarized in Table 1. The age of onset can be relevant as adverse food reactions are

Table 1. Possible clinical manifestations of adverse food reactions

Dermatological	Gastrointestinal	Respiratory
Non-seasonal pruritus	Increased daily bowel movements (> 3)	Sneezing associated with eating
Secondary infections (pyoderma, Malassezia overgrowth)	Poor fecal consistency	Reverse sneezing
Otitis (acute, recurrent, chronic)	Chronic or intermittent diarrhea	Conjunctivitis
Urticaria	Vomiting	Asthma
Angioedema	Gas	Anaphylaxis
Perineal fistula	Belching	
Onychodystrophy	Borborygmi	
Barriers to food intake	Weight loss	

more common in young dogs (<1 year) or older dogs (>6 years).[15] Pinpointing when the problem started could be challenging due to the owner's inability to identify early or more subtle symptoms.

A complete physical exam should always be performed, and a careful dermatological evaluation includes necessary tests that help narrow the diagnosis: cytology, trichogram, Wood's lamp, and skin scraping. Additionally, bacterial or mycological cultures, biopsies, and blood testing might be required in some patients. A thorough nutritional assessment, including a thorough nutritional history, should also be obtained before starting a food elimination trial. The nutritional history should include all past diets and proteins consumed, if possible. Obtaining this diet history will allow for the selection of an appropriate diet and an accurate diagnostic trial.

In dogs, the most commonly reported dietary allergens include beef, chicken, dairy, and wheat, while in cats, the most frequent allergens are beef, chicken, and fish.[16] Published studies regarding allergens are infrequent and have varying criteria for diagnosing and confirming offending allergens; some of these studies are now quite old. For example, fish allergy in dogs is probably more common than has been reported.[17] It is important to realize that animals become allergic to what they eat regularly; signs of allergy are not usually seen on the first exposure to a food. More research is needed using the more homogenous criteria that have been proposed recently.[18] Generally, animal proteins are considered the most common food allergens in dogs and cats. It's also important to consider the possibility of cross-reactivity between different antigens in animal protein (fish-chicken and between mammalian proteins), as described in the literature.[19] This is especially important to consider when choosing a diagnostic diet.

The diagnosis of adverse food reactions requires a dedicated food trial. While several commercial tests are offered directly to the client or veterinarians, they are unreliable for diagnosis, and results are inconsistent.[20] Prior to the initial consult, some owners will have performed testing and believe in the results; it is important to take the time to talk about the need to complete a food elimination trial to confirm the diagnosis. Always consider it is best not to make owners feel bad about previous diagnostic and treatment efforts.

Talking about feeding and diets can be challenging because it is a personal and emotional subject for many owners; developing skills and good strategies can be highly rewarding to obtain accurate information and create a receptive environment to recommend a diagnostic diet when needed.[21] Many owners visiting their veterinarian for a skin condition will assume their pet has a food allergy regardless of the signs. These owners may have already changed the food they are

feeding and, in some cases, have tried many different proteins and types of diets; choosing a novel protein for a diagnostic food elimination trial in such patients will be more difficult. Also, realistically a detailed feeding history will often only include some of the different foods the pet owner has fed their pet. It is important to consider that some owners will be reluctant to use commercial diets because of the dangers perceived related to commercial foods.

Successful food elimination trials require good communication skills. Listening to the pet owner to understand their needs and concerns goes a long way when choosing the right type of diet that will also be a good choice for the patient.[21] Under certain circumstances, a food elimination trial cannot be performed correctly. It will result in a loss of time and money and become frustrating. Consider that pets in homes with small children or multiple pets, where hunting or scavenging food is possible, or with owners who are elderly or unable to follow instructions are not good candidates for a food elimination trial.

Food elimination trials in cats can be especially challenging as they are more sensitive to diet changes, and refusing new diets is more common. Cats should never be starved when trying to change their diet. Also, consider that cats that can go outdoors, access other foods, and hunt will not be good candidates for a food elimination trial; keeping them inside can be extremely difficult.

Choosing the correct type of diet is important. Hydrolyzed or amino acid-based diets (elemental diets, dogs only) are often considered the best choices for diagnostic trials. Novel protein diets are also available for food elimination trials but may result in cross-reactivity concerns, may conflict with proteins commonly found in well-pet diets, and require a very thorough nutritional history to select a diet that will enable success. Choosing a suitable novel protein can be difficult. Hydrolyzed and amino acid-based diets are manufactured in controlled conditions where cross-contamination is avoided, are complete and balanced, and have lower antigenic potential because of the hydrolysis process and/or the ingredients they contain.[22,23] No universal diet will work for all patients; palatability can be an issue for some pets using hydrolyzed diets. Some patients may require more than one food elimination trial to make a diagnosis. Diet selection may be more challenging in patients with concurrent conditions such as pancreatitis, and nutritional information such as calorie information and nutrient content should be used to guide diet selection. In some cases, nutritional limitations make it very difficult to find a suitable diet for a food elimination trial.

Non-declared ingredients can be problematic, especially when using well-pet diets.[24,25] Home-cooked diets can be used for food elimination trials, or when other diseases are also present, but ingredients should be carefully selected. When considering special dietary requirements in the patient, a board-certified veterinary nutritionist is recommended to ensure proper nutrition. Home-prepared or commercially available raw diets are not recommended due to the potential health risks associated with their use. Several studies and publications have demonstrated danger to dogs or cats and a public health risk.[26] Clients should also be informed about the possibility of commercial raw diets containing ingredients not included on the label, and that they may not be complete and balanced.[27] We should keep in mind that people using raw diets tend to have less confidence in veterinary advice and may be more challenging to educate.[28]

Once the diet selection is made, the implementation should be discussed; essential topics to discuss with pet owners when starting a food elimination trial are listed in **Table 2**. Most importantly, the owner should understand the purpose of the diet and the trial, and why it is essential to determine what role the diet plays in their pet's problems.

Itching, otitis, and secondary infections must be addressed when initiating the food elimination trial; having uncontrolled infections and pruritus will reduce the chances of a successful food elimination trial and,

COMMUNICATION TIP

Owners should be instructed on what to expect during the challenge portion of the food elimination trial, what signs to look for, and to stop if signs occur.

Table 2. Essential considerations to discuss with pet owners when starting a food elimination trial

How to introduce the diet	Gradual introduction of the new diet Palatability considerations (enticers are not permitted, but water or some oils can be used)
What changes could be expected to happen	Explain that changes such as stool consistency and frequency could occur, particularly with hydrolyzed or amino acid-based diet
What to monitor and report	Vomiting, diarrhea, refusing the food, any skin issues that are not resolving or worsening
Trial duration	Dogs 4-12 weeks Cats 4-6 weeks Individual adjustments are always necessary, and owners should be made aware.
How and when to reach out for help	Instructions should include messaging or voice contact options; good communication will help avoid time loss and treatment errors.
Time for a recheck	The patient should have an appointment made for a next visit so that skin treatment can be adjusted and diet modification can be recommended in a timely fashion.
Medications, supplements, and treats	Flavored medications, supplements, and treats should be discontinued, and alternatives found when necessary.
Written instructions	Complete information about diet trials, duration, and most details should be provided so owners can go over the instructions at home and ask additional questions. This can be done as a handout, a video, or a digital link.
Other diet-related instructions	Treats or canned foods from different formulas than the one being used as the main diet should be avoided.

more importantly, recognition of improvement gained with the diet. Untreated ear infections will continue to cause discomfort regardless of the diet selected.

Some cases will get stuck in the trial phase for months because of interruptions such as feeding other foods by accident or because someone in the household keeps feeding the patient other foods. Flavored medication, finding food, licking plates in the dishwasher when left open, and other situations may also be concerns in certain cases. Another common reason is failing to return for a recheck because owners believe a treatment and solution has been found without diet challenges. Client communication is a key part of a successful food elimination trial.

The food elimination trial should typically last 4-12 weeks in dogs and 4-6 weeks in cats, but it is crucial to recognize that adjustments for each patient are necessary.[29] For patients with gastrointestinal signs alone, the food elimination trial can be shorter (2-4 weeks total), and patients should show signs of improvement within the first two weeks. When using medications such as steroids or oclacitinib, a shortened trial can be attempted with success depending on the response and control of symptoms that are achieved.[30] In cases where an adverse food reaction is highly suspected, but the first trial is unsuccessful, a second or third food elimination trial with a different diet might be attempted if the owner is willing and compliance can be maintained.

When itch control medication is prescribed, it should be suspended after a few weeks on the food elimination trial when skin conditions have improved in order to evaluate itch level and patient improvement. Pruritus does not have to resolve completely to consider that the diet has benefited the patient; some will have environmental allergies that also contribute to their symptoms.

Challenging the diet is required to confirm that improvement in the patient is related to the new diet; sometimes, owners will be wary of this part of the process, particularly in now well-controlled patients. At this time, explaining the value of a challenge is important after several weeks of significant effort. Having an answer to the role of the diet can be very

rewarding instead of having an unexplained flare and having to restart the food elimination trial.

Diet challenges can be performed using the diet that the pet was fed before, or they can be performed using individual food antigens, usually animal proteins. Owners should be instructed to challenge with one ingredient at a time when using this approach. Usually, the author will challenge with a single allergen every two weeks to identify any reaction before starting a new ingredient. Management of cats and dogs with adverse food reactions will require long-term allergen avoidance.

When initiating a challenge, owners should be informed of possible signs of a reaction; in a recent study, paw licking and itching was the most common behavior detected, and most flares occurred in the first 72 hours of the challenge.[31] Delayed reactions can present up to 14 days after the challenge.[32] Some reactions can be very evident, but others can be subtle, and ideally, owners should be instructed on what to expect. Signs of a positive challenge can include erythema, papules, increased pruritus, head shaking, rubbing, chewing, and biting. Owners should know to stop the challenge, return to the food elimination trial food, and, if necessary, when to contact the veterinary team to seek help if medication is needed to control the flare. Ideally, the veterinary team would want patients to have another reduction of clinical signs on the diet chosen initially for the trial, and this would confirm the diagnosis.

Once a cutaneous adverse food reaction has been confirmed, management of cats and dogs will require long-term allergen avoidance. Most importantly, tailoring to every patient's needs is necessary. For long-term management, the diet used for the elimination trial can be used indefinitely or until other medical problems affecting diet selection arise, but some clinicians opt to change the patient to a different hydrolyzed or novel protein diet. Although patients may not have the same response to a different diet, benefits of a diet change after completion of a successful trial include cost to the owner and potential management of multiple conditions. Some patients' signs will resolve completely after a successful trial; however, others might require additional diagnostic testing and therapies, such as testing for allergen-specific immunotherapy. Multimodal management for the allergic dog or cat is still the best approach considering medical, topical, and nutritional interventions for all conditions present, including adverse food reactions but also atopic dermatitis, secondary infections, and other concurrent problems. Please refer to the practical tool following this chapter for additional information.

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PRACTICAL TOOL: DIAGNOSIS AND MANAGEMENT OF POTENTIAL CUTANEOUS ADVERSE FOOD REACTIONS

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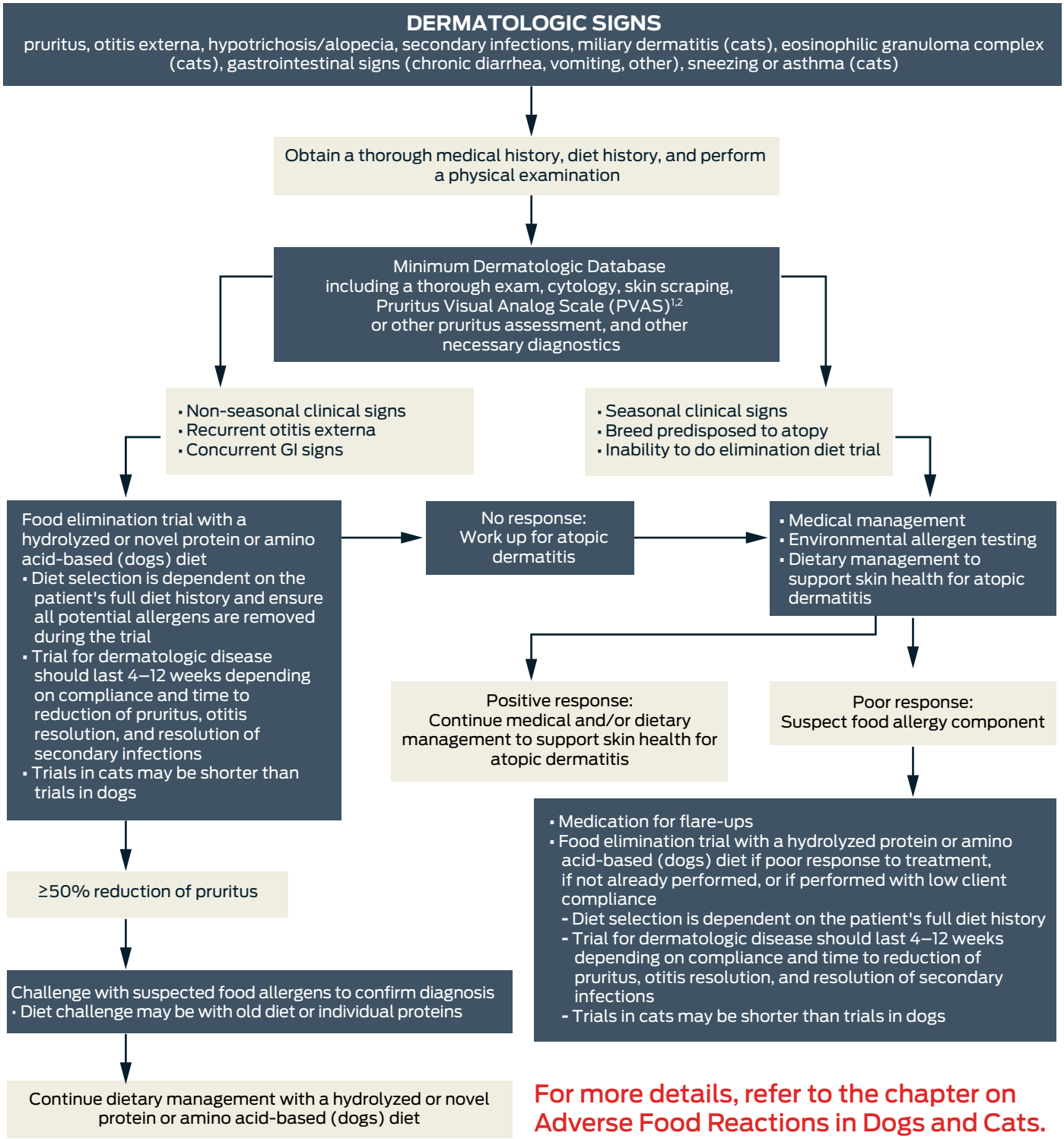

For more details, refer to the chapter on Adverse Food Reactions in Dogs and Cats.

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ATOPIC DERMATITIS IN DOGS AND CATS

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KEY TAKEAWAYS

- Essential fatty acids and other nutritional modifications may be beneficial as adjunct treatment for atopic dermatitis in dogs and cats.
- Atopic dermatitis and cutaneous adverse food reaction (food allergy or intolerance) may have similar clinical signs and exist concurrently.

OVERVIEW

This chapter will explain how nutrition may influence atopic dermatitis in dogs and cats. Canine atopic dermatitis (cAD) is defined as genetically determined inflammatory and pruritic skin disease with an immune response against environmental allergens.[1] In cats, atopic dermatitis may be referred to as feline atopic skin syndrome (FASS), an inflammatory and pruritic skin syndrome of cats manifested by a spectrum of reaction patterns, and that may be associated with IgE antibodies to environmental allergens.[2] In both species the diagnosis of atopic dermatitis is one of exclusion (**Figure 1)**, following published criteria of clinical signs and resolving other confounding factors, such as bacterial or fungal skin infections, ectoparasite infestation or allergy, and food allergy (cutaneous adverse food reaction [CAFR]).[3-5] The latter factor is sometimes referred to as 'food-induced atopic dermatitis';[6,7] however, as there is a separate chapter in this book on adverse food reactions, that particular influence of nutrition on clinical signs will not be discussed here.

Attempts to influence the severity of pruritus, inflammation, and the degree of improvement as perceived by both the research veterinarian and the owner have investigated four dietary modifications: changing the diet, adding essential fatty acids (EFAs), adding palmitoylethanolamide (PEA), and adding probiotics. The various references often have used different modalities of evaluating efficacy of diets or supplements. This is especially true in publications prior to 1997 as that year saw the first report of the Canine Atopic Dermatitis Extent and Severity Index (CADESI), which evaluated lesions in dogs with cAD and has gone through several iterations, with the number of the iteration noted following a hyphen (example CADESI-1).[8] Further evaluation systems and their initial published use include the Canine Atopic Dermatitis Lesion Index (CADLI, 2007)[9] and in cats, Scoring Feline Allergic Dermatitis (SCORFAD, 2012) and Feline Dermatitis Extent and Severity Index (FeDESI, 2015).[10-12] In many of the more recent studies, owners were asked to evaluate the decrease in pruritus using a pruritic visual analogue scale (pVAS).[13] It is important to understand the difference between veterinarian evaluation modalities (CADESI, CADLI, SCORFAD, and FeDESI) as these evaluate *lesions*, while the owner evaluation via pVAS uses the owner's perception of the severity of *pruritus*. Because of these varying modalities, accurate comparison of various studies may be difficult.

DIETARY CHANGES

When supplements such as omega-3 and omega-6 EFAs are included in the dog food, the success rate in one open trial was 42% (good to excellent control of pruritus),[14] and in another trial it was 44%.[15] In this latter trial, dogs responding to the test diet had a different pattern of fatty acid change in the plasma and the skin as compared with the dogs that failed to respond to the diet, suggesting that there are subsets of atopic dogs with different fatty acid metabolism capabilities.[15] Somewhat in contrast, another article noted that the improvement seen in atopic dogs with EFA supplementation did not seem to be correlated with total fatty acid intake or with the ratio of omega-6:omega-3 fatty acids in the diet.[16] Another report documented improvement in the CADESI-2 score by the use of a dog food enriched with EFAs in an omega 6:3 ratio of 5. However, no dog had an improvement of 50% or greater in the CADESI-2 score, and only 2 dogs of the 16 that completed the study showed an improvement of

more than 50% in the pVAS, showing the sometimes noted disconnect between the CADESI and the pVAS.[17] Another report documented improvement in pruritus and/or CADESI-3 scores when atopic dogs were fed three different commercial diets that were formulated for allergic dogs.[18] Two of these diets were fish-based; the third had hydrolyzed chicken and soy as its protein components. While the specific claims of these diets to being formulated for allergic dogs were not delineated, all three had greater levels of both omega-6 and omega-3 EFAs than the control diet.[18] However, in a systematic review of randomized controlled trials for prevention or treatment of atopic dermatitis in dogs, the conclusion in regard to these two reports is that there was only low-quality evidence of efficacy of a commercial diet as a glucocorticoid-sparing intervention.[19]

More recent diet trials showed similar possibilities as adjunctive therapy for atopic dermatitis. In a comparison of two EFA-enriched commercial diets, using validated scoring systems, mild improvement was seen in lesions, pruritus, and coat quality in both diets after 12 weeks.[20] In a non-controlled, open-label clinical trial of a diet with added polyunsaturated fatty acids (PUFAs), polyphenols, and antioxidants, veterinary assessments of CADESI-3 scores showed a significant decrease at 4 and 8 weeks of feeding the diet to 17 dogs with atopic dermatitis. Similarly, owners' assessments of pruritus (licking/scratching) and erythema showed significant improvement.[21] Continuing the investigation of a diet with added PUFAs, polyphenols, and antioxidants, in a randomized, double-blind, placebo-controlled clinical trial, there were significant improvement in CADESI-4 scores and owner-reported pruritus scores.[22]

Finally, in a very recent study, a standard kibble test diet was contrasted with the same kibble diet to which were added additional omega-3 EFAs (including linoleic acid [LA], eicosapentaenoic acid [EPA], and docosahexaenoic acid [DHA]), licorice root extract, and turmeric extract. Pruritus, CADESI-4 score, and adjunctive medication needed were evaluated. There was a significant improvement in the pruritus score as well as a reduced medication requirement for dogs receiving the therapeutic diet after 3 months, the latter becoming significant at 6 and 9 months.[23] While the CADESI-4 scores decreased more in the dogs fed the supplemented diet kibble, the difference was not significant.

ESSENTIAL FATTY ACIDS

The following studies looked at adding EFAs as separate supplements to dogs or cats already on balanced diets. Early studies used evening primrose (*Oenothera biennis*) oil (EPO) and/or marine fish oil as a source of omega-6 or omega-3 EFAs. In one study, 10 of 21 dogs that were already well-controlled on a combination EPO and fish oil supplement were switched to olive oil (which does not contain omega-6 or omega-3

Table 1. Primary EFA contents of oils and essentiality

Supplement	Primarily omega-3 or -6	Name
Marine fish oil (salmon, sardine, anchovy, herring, or mackerel)	omega-3, essential	eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)
Evening primrose oil *Oenothera biennis*	omega-6, nonessential	gamma-linolenic acid (GLA)
Borage seed oil *Borago officinalis*	omega-6, nonessential	gamma-linolenic acid (GLA)
Black currant oil *Ribes nigrum*	omega-6, nonessential	gamma-linolenic acid (GLA)
Flaxseed oil *Linum usitatissimum*	omega-3, essential (dogs) or conditionally essential (cats)	alpha-linolenic acid (ALA)
Corn oil *Zea mays*	omega-6, essential	linoleic acid (LA)
Olive oil *Olea europaea*	neither (primarily monounsaturated fatty acids)	oleic acid
Sunflower oil *Helianthus annuus*	monounsaturated fatty acids, omega-6, oleic acid = nonessential; LA = essential	oleic acid, linoleic acid (LA)

fatty acids) as a placebo. The clinical condition of 8 of the 10 dogs switched from EPO/fish oil to olive oil deteriorated over the 8-week course of the study, whereas only 2 of the 11 dogs that were maintained on the original supplement had a worsening of clinical signs.[24] In a 3-week cross-over study, marine (fish) oil or corn oil as placebo was given to dogs with idiopathic pruritus, confirmed atopy, and/or flea allergy. The dogs receiving the marine oil had significantly less pruritus and alopecia, and better coat quality.[25] Another study compared the efficacy of marine fish oil, EPO, and two commercial EFA supplements in 20 dogs with either atopic dermatitis or idiopathic pruritus, and found that five dogs had a good-to-excellent reduction in their level of pruritus with at least one of the products.[26] In another early, double-blind, placebo-controlled study of the effect of EPO on non-seasonally-affected atopic dogs, erythema but not pruritus was significantly reduced.[27]

COMMUNICATION TIP

"Diets with added EFAs, EFAs given separately, or PEA supplementation may have beneficial effects as adjunctive treatment in dogs and cats with atopic dermatitis."

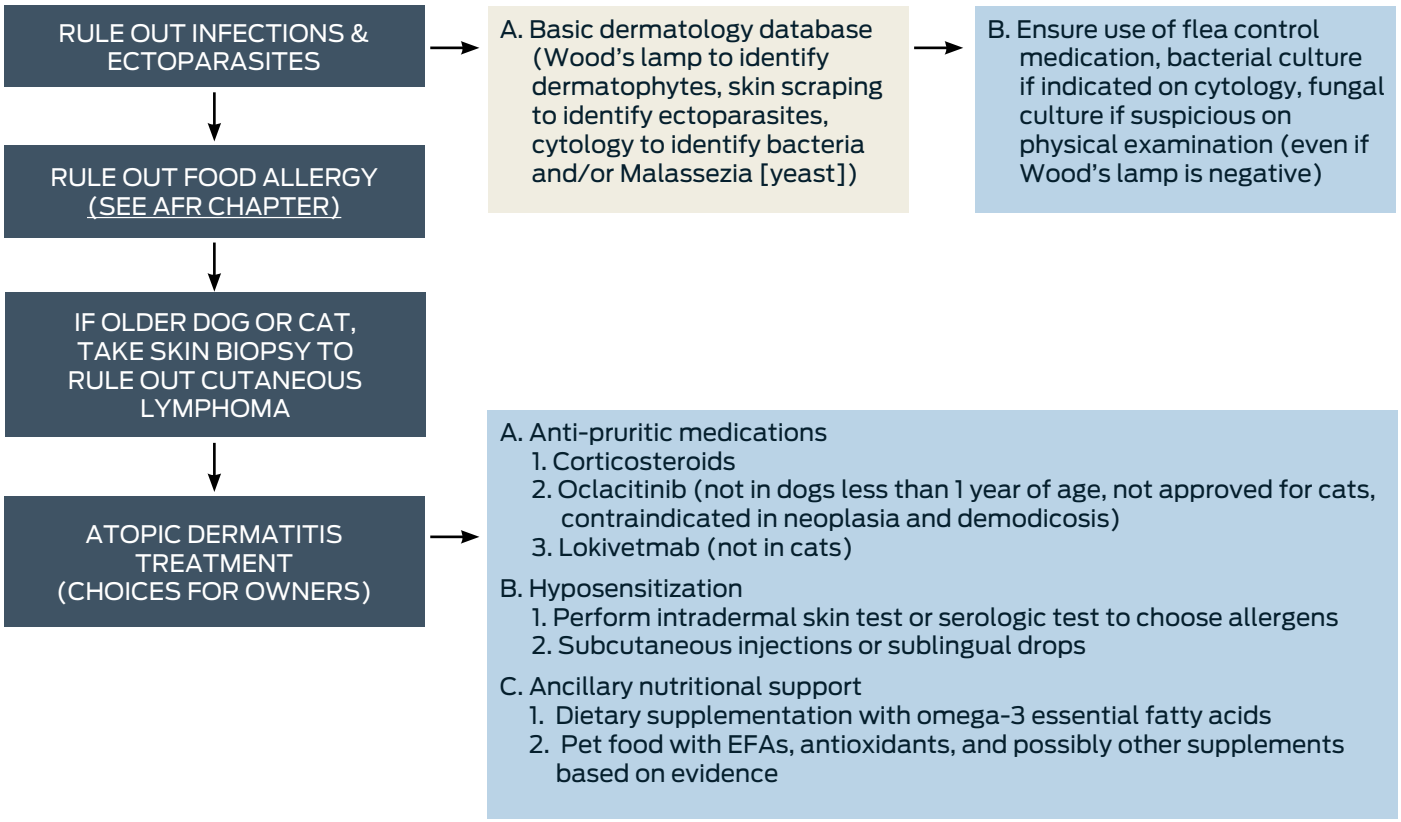
In a later study, dogs were given a supplement containing EPA, DHA, and gamma-linolenic acid (GLA) with an omega-6 to omega-3 ratio (including diet) of 5.5:1. Atopic dogs of two stages of severity were considered: an early stage "pre-immunotherapy" (15 cases), which included dogs not yet exposed to any treatment and a late stage "post-immunotherapy" (7 cases), which included dogs with chronic atopic dermatitis on immunotherapy but not yet responsive. The early stage dogs responded with 53% (8 of 15) having a good effect on pruritus management, while only 1 of 7 (14%) later stage dogs improved. This may have been due to the chronicity of the lesions, secondary infections, or differences in the metabolism of the EFA, as serum arachidonic acid (AA) was significantly lower at the end of the trial in the early stage dogs, while GLA was significantly higher in the later stage dogs.[28] A very recent study gave atopic dogs, already shown not to have food allergy, a hypoallergenic diet and a nutraceutical containing black currant seed oil (a source of GLA and alpha-linolenic acid [ALA]), *Lactobacillus reuteri*, and zinc. CADLI scores and pVAS scores showed a statistically significant decrease after 60 days. After 60 days, the nutraceutical was discontinued, and the scores showed a non-statistically significant increase over another 60 days.[29]

Another report documented the clinical effects of EFAs in some atopic dogs. Over a 12-week trial, atopic dogs were given either a mix of borage oil (high in GLA) and fish oil or a placebo, in addition to prednisolone. Owners monitored pruritus daily with a pVAS score, and the investigators graded the clinical signs at 0, 42, and 84 days. While both groups of dogs' pruritus scores decreased over time, at 64 days the decrease became significantly lower in the borage/fish oil dogs, with an increasing difference over the rest of the trial. Both the use of prednisolone and the skin lesion score were lower in the borage/fish oil group, though these were not significant.[30]

In cats, most reports date back several decades, with cats manifesting clinical signs of atopic dermatitis (pruritus and miliary dermatitis [papules and crust]) but not necessarily having a diagnosis of food allergy and/or flea allergy eliminated.[31-34] In one double-blind study comparing EPO versus olive oil as a control, there was no significant difference in clinical signs between the two oils after 8 weeks.[31] In a study from the UK using cats with miliary dermatitis, EPO was compared with sunflower oil. Both EPO and sunflower ameliorated clinical signs, but upon discontinuation, the cats that had received the EPO "deteriorated" less than those receiving sunflower oil.[32] In a sister study that compared EPO alone, fish oil alone, and a combination of EPO and fish oil, cutaneous signs improved when the cats were supplemented with either EPO alone or with a combination of EPO and fish oil. Fish oil did not maintain remission of clinical signs by itself.[33] In another study, 3 out of 5 cats with miliary dermatitis had their skin lesions resolve entirely upon being administered oral omega-3 EFAs.[34]

It is important that the omega-3 fatty acids in the diet are considered before supplementing additional omega-3, in order not to exceed the NRC safe upper limit (SUL) for EPA+DHA of 280 mg/100 kcal for adult dogs. The NRC has not yet established an SUL for cats so caution should be used.[35]

Figure 1. A stepwise process to diagnosing and treating atopic dermatitis



PALMITOYLETHANOLAMIDE (PEA)

Palmitoylethanolamide is a naturally occurring bioactive lipid and endocannabinoid-like molecule produced on demand by damage-exposed cells, and has been documented to counteract inflammation, itch, and pain.[36] PEA levels were increased in atopic dogs' skin compared with healthy controls.[37] In another study, palmitoylethanolamide ultra-micronized (PEAum) was given to 160 nonseasonal atopic dogs over a 56-day period at a dose approximating to 10 mg/kg, with lesions and pruritus monitored with CADLI and pVAS, respectively. Of the 122 dogs that completed the study, 62% reached a CADLI score indicative of remission; 35% showed a 50% or greater decrease in pruritus.[38] In a similar, double-blind, multicenter, randomized, placebo-controlled study in cats without flea allergy, PEAum at a dose approximating to 15 mg/kg was compared with a placebo in the ability to maintain remission that was induced by a tapering methylprednisolone dose. Using both pVAS and SCORFAD, the average worsening of pruritus at the end of the study was lower in the PEAum group compared with placebo (P = 0.04), whereas SCORFAD was not different, again noting the potential disconnect between pruritus and lesions.[39] In a systematic review of treatments for feline atopic syndrome (which includes feline atopic skin syndrome [FASS]), the evidence pointed to low-to-moderate efficacy for fatty acids and PEA.[40] PEA may not be available or approved by regulatory agencies in all countries, and it may be regulated differently depending on the country.

PREVENTION OF ATOPIC DERMATITIS WITH DIET

There have been several attempts to investigate the role of diet in young dogs in order to prevent the onset of canine atopic dermatitis (cAD). In an early study, feeding a diet including homemade or noncommercial products to the bitch during lactation seemed to have a protective effect on the development of cAD in the offspring; the odds of developing cAD were twice as high among offspring from bitches that were not exposed to homemade/noncommercial diets.[41] The reason for this difference is not understood and does not decrease the importance of feeding a complete and balanced diet, especially during a demanding life stage such as lactation. If homemade diets are fed at any life stage, a board-certified veterinary nutritionist should be involved in the formulation.

Another study looked at pups that had been epicutaneously sensitized to the house dust mite *Dermatophagoides farina* (Df). Both the bitch during pregnancy and the pups from 3 weeks to 6 months of age were administered the probiotic *Lactobacillus rhamnosus* strain GG. This appeared to reduce immunologic indicators of cAD (serum titers of IgE and response to intradermal testing of Df), although no significant decrease in clinical signs was detected.[42] A follow-up study three years later showed that early exposure to *Lactobacillus rhamnosus* GG significantly decreased allergen-specific IgE and partially prevented cAD in the first 6 months of life.[43] However, exposure to the *L. rhamnosus* strain GG early in life did not alter the expression of filaggrin (an important component of the stratum corneum) in this experimental cAD model, suggesting its beneficial effects had other mechanisms.[44]

In another study pregnant bitches and their subsequent litters were fed either supplemented or unsupplemented diets. Nutrients supplemented were nicotinamide (niacinamide), pantothenate, histidine, inositol, and choline. Circulating IgE levels to dust mite allergens Der f and Der p were measured when the puppies were 6 and 12 months old. Two owner questionnaires were used to assess the occurrence of typical signs associated with atopic dermatitis when dogs were between the ages of 22 and 36, and 34 and 48 months. Higher levels of circulating anti-Der f and anti-Der p IgE during the first year were found in the dogs fed the unsupplemented diet. The owner-assessed incidence of atopic dermatitis signs among the dogs was significantly greater in the unsupplemented group at the time of the second follow-up questionnaire. These outcomes suggested that the nutrients supplemented allowed for an improvement to barrier function early in life and may reduce the frequency of signs associated with atopic dermatitis.[45] Finally, in one study from Finland, puppyhood exposure to raw animal-based foods might have a protective influence on owner-reported allergy/atopy skin signs (AASS) in adulthood, while puppyhood exposure to mixed oils, heat-processed foods, and sugary fruits might be a potential risk factor for developing those signs. The study suggests a causal relationship but does not prove it.[46] The study's reliance on an owner response survey, as well as other methodology, has been critiqued.[47,48]

FUTURE AREAS OF RESEARCH FOR ATOPIC DERMATITIS AND NUTRITION

In addition to the above noted research with *Lactobacillus rhamnosus* strain GG, other reports with probiotics in cAD noted varying results.[49-51] Studies have not been published in cats as of the time of writing this chapter. The use of probiotics in the management of atopic dermatitis is a future area of research in dogs and cats.

CONCLUSIONS

Nutrition can be an important part of management for dogs and cats with atopic dermatitis. Diets with added EFAs, EFAs given separately, or PEA supplementation may have beneficial effects as adjunctive treatment in dogs and cats with atopic dermatitis. Omega-3 EFAs (EPA and DHA) may be the most beneficial. The role of these and other foods, specific ingredients, and other supplements in possibly preventing or delaying the occurrence of atopic dermatitis deserves further study. Atopic dermatitis and CAFR may have similar clinical signs and exist concurrently; thus it is important to determine if CAFR is present in order to definitively diagnose atopic dermatitis (**Figure 1**).[52,53]

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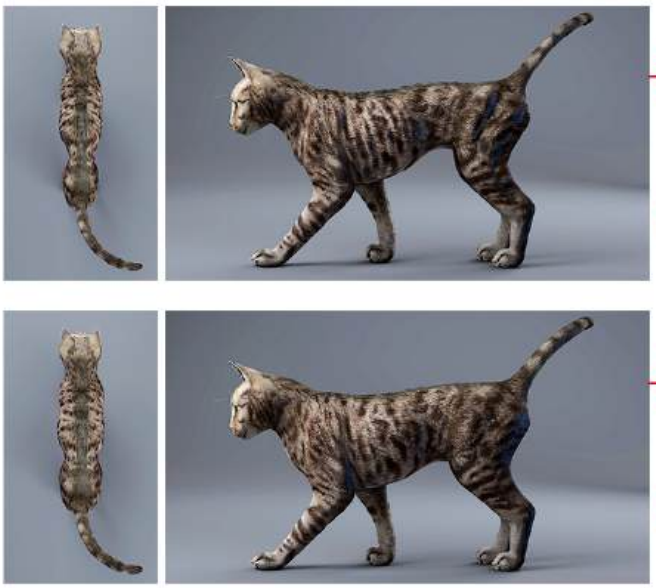
Advancing Science for Pet Health

ENDOCRINE AND METABOLIC DISORDERS

BODY CONDITION SYSTEM

TOO THIN

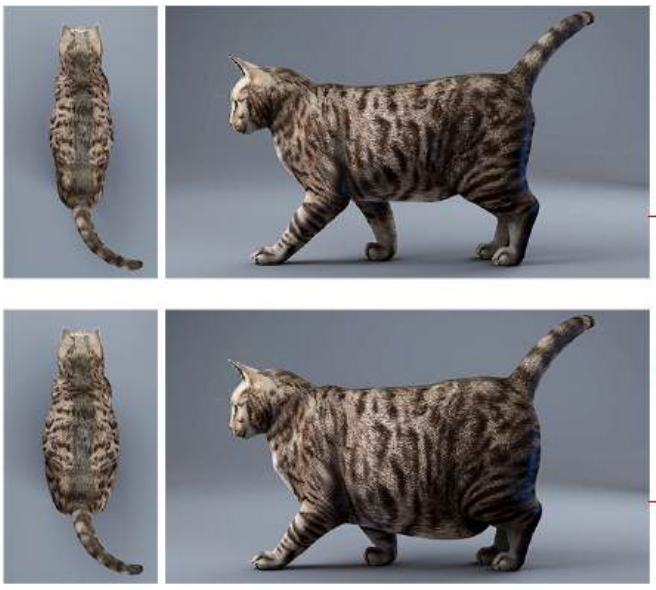


1. Ribs visible on shorthaired cats; no palpable fat; severe abdominal tuck; lumbar vertebrae and wings of ilia easily palpated.
2. Ribs easily visible on shorthaired cats; lumbar vertebrae obvious with minimal muscle mass; pronounced abdominal tuck; no palpable fat.
3. Ribs easily palpable with minimal fat covering; lumbar vertebrae obvious; obvious waist behind ribs; minimal abdominal fat.
4. Ribs easily palpable with minimal fat covering; noticeable waist behind ribs; slight abdominal tuck; abdominal fat pad absent.

IDEAL

5. Well-proportioned; observe waist behind ribs; ribs palpable with slight fat covering; abdominal fat pad minimal.

TOO HEAVY



6. Ribs palpable with slight excess fat covering; waist and abdominal fat pad distinguishable, but not obvious; abdominal tuck absent.
7. Ribs not easily palpated with moderate fat covering; waist poorly discernible; obvious rounding of abdomen; moderate abdominal fat pad.
8. Ribs not palpable with excess fat covering; waist absent; obvious rounding of abdomen with prominent abdominal fat pad; fat deposits present over lumbar area.
9. Ribs not palpable under heavy fat cover; heavy fat deposits over lumbar area, face and limbs; distention of abdomen with no waist; extensive abdominal fat deposits.

The BODY CONDITION SYSTEM was developed at the Nestlé Purina Pet Care Center and has been validated as documented in the following publications:

Laflamme, D. P. (1997). Development and validation of a body condition score system for cats: A clinical tool. *Feline Practice*, 25(5-6), 13-18.
German, A. J., Holden, S. L., Moxham, G. L., Holmes, K. L., Hackett, R. M., & Rawlings J. M. (2006). A simple, reliable tool for owners to assess the body condition of their dog or cat. *Journal of Nutrition, 136*(7 Suppl), 2031S-2033S. doi: 10.1093/jn/136.7.2031S
Bjornvad, C. R., Nielsen, D. H., Armstrong, P. J., McEvoy, F., Hoelmkjaer, K. M., Pedersen G. F., & Kristensen, A. T. (2011). Evaluation of a non-point body condition scoring system in physically inactive pet cats. *American Journal of Veterinary Research, 72*(4), 433-437. doi: 10.2460/ajvr.72.4.433

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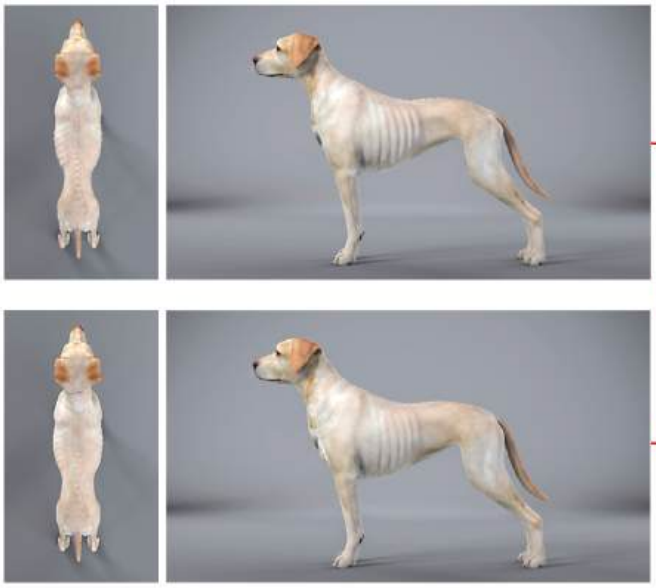
Advancing Science for Pet Health

BODY CONDITION SYSTEM

TOO THIN

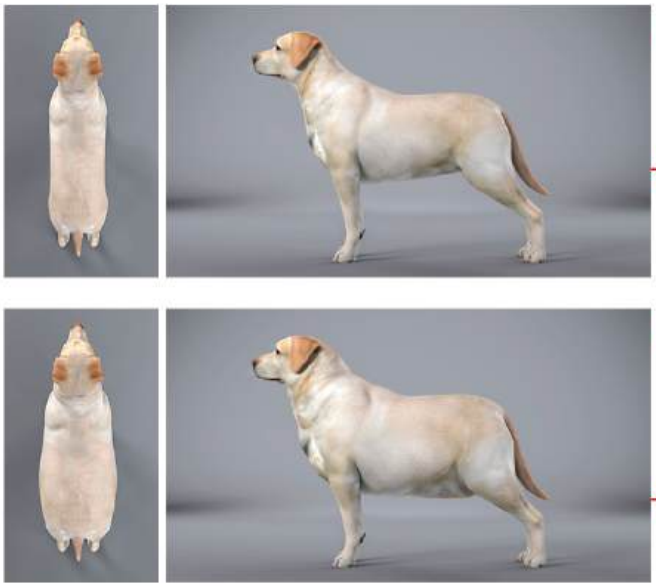


1. Ribs, lumbar vertebrae, pelvic bones and all bony prominences evident from a distance; no discernible body fat; obvious loss of muscle mass.
2. Ribs, lumbar vertebrae, pelvic bones easily visible; no palpable fat; some evidence of other bony prominence; minimal loss of muscle mass.
3. Ribs easily palpated and may be visible with no palpable fat; tops of lumbar vertebrae visible; pelvic bones becoming prominent; obvious waist and abdominal tuck.

IDEAL

4. Ribs easily palpable, with minimal fat covering; waist easily noted when viewed from above; abdominal tuck evident.
5. Ribs palpable without excess fat covering; waist observed behind ribs when viewed from above; abdomen tucked up when viewed from the side.

TOO HEAVY



6. Ribs palpable with slight excess fat covering; waist is discernible viewed from above, but is not prominent; abdominal tuck apparent.
7. Ribs palpable with difficulty; heavy fat cover; noticeable fat deposits over lumbar area and base of tail; waist absent or barely visible; abdominal tuck may be present.
8. Ribs not palpable under very heavy fat cover, or palpable only with significant pressure; heavy fat deposits over lumbar area and base of tail; waist absent; no abdominal tuck; obvious abdominal distention may be present.
9. Massive fat deposits over thorax, spine and base of tail; waist and abdominal tuck absent; fat deposits on neck and limbs; obvious abdominal distention.

The BODY CONDITION SYSTEM was developed at the Nestlé Purina Pet Care Center and has been validated as documented in the following publications:

Laflamme, D. P. (1997). Development and validation of a body condition score system for dogs: A clinical tool. *Canine Practice*, 22(4), 10-15.

Mawby, D. I., Bartges, J. W., d'Avignon, A., Laflamme, D. P., Moyers, T. D., & Cottrell, T. (2004). doi: 10.5326/0400109

German, A. J., Holden, S. L., Moxham, G. L., Holmes, K. L., Hackett, R. M., & Rawlings J. M. (2006). A simple, reliable tool for owners to assess the body condition of their dog or cat. *Journal of Nutrition*, 136(7 Suppl), 2031S-2033S. doi:10.1093/jn/136.7.2031S

German, A.J., Holden, S. L., Morris, P. J., & Biourge, V. (2010). Comparison of a bioimpedance monitor with dual-energy x-ray absorptiometry for noninvasive estimation of percentage body fat in dogs. *American Journal of Veterinary Research*, 71(4), 393-398. doi: 10.2460/ajvr.71.4.393

OVERWEIGHT AND OBESITY IN DOGS AND CATS

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KEY TAKEAWAYS

- Practical resources and published guidelines can support the development and implementation of weight management plans for dogs and cats.
- A full nutritional assessment of the pet, family, and human–animal bond can help tailor weight management plans to set families up for success.
- Conversations and goals that focus on quality of life can support how families enjoy their relationship with their pet and improve acceptance and adherence.

DEVELOPING AND IMPLEMENTING WEIGHT MANAGEMENT PLANS FOR DOGS AND CATS

Many practical resources including guidelines and algorithms are available with step-by-step details for developing weight loss plans for dogs and cats.[1-3] While developing and implementing weight management plans, including important aspects of each family's unique human–animal bond can individualize plans to each owner-pet relationship and increase adherence.[4] Key components of weight management plans are summarized in **Box 1**. These components utilize available guidelines to tailor weight loss plans, setting families up for success.

1. Full Nutritional Assessment of Animal, Human, Diet, and Environment Factors

A full nutritional assessment, as described in the 2021 American Animal Hospital Association (AAHA) Nutritional and Weight Management Guidelines,[2] will provide a comprehensive assessment of the pet, family, diet, and environment to best guide conversations and identify effective strategies for each unique pet and family.

Strategies for success: Dr. Churchill describes the stages of 'readiness to change' and how to apply this theory to veterinary weight loss cases.[5] This concept of assessing how ready families are to change can guide realistic goals and conversations. This then allows families time to reflect so they engage in weight loss interventions when they are ready and committed (and thus also more likely to be successful).

2. Determination of Nutritional Goals and Key Nutrients of Concern

Nutritional goals, informed by the prior assessment, should be individualized for each pet, including any medical conditions or any unique essential needs of that particular animal.[2] Key nutrients of concern should include those necessary for optimal health during caloric restriction, modification due to other co-morbidities, and those that align with desired preferences and lifestyle needs of pet and family. Examples for otherwise healthy pets are summarized in **Table 1**. Most important, nutrient density should be evaluated to reduce risk of malnutrition in order to reduce calories without restricting important nutrients,[6-8] with emphasis on adequate protein for maintenance of lean body mass during restriction and for satiety.[9-11] Increased owner satisfaction and dog or cat enrichment may promote positive behaviors from both a pet owner and a pet perspective. More detailed

Box 1. Key components of weight management plans for cats and dogs

1. Full nutritional assessment of animal, human, diet, and environment factors
2. Determination of nutritional goals and key nutrients of concern
3. Selection of appropriate diet and treat options
4. Creating an initial calorie goal
5. Monitoring and adjustment of goals
6. Behavioral management and troubleshooting

Table 1. Key nutrients of concern for otherwise healthy dogs and cats undergoing caloric restriction

Key nutrients of concern	Typical strategy during weight loss	Evidence-based medicine: goals and supportive guidelines and studies
Nutrient density or nutrient:calorie ratio	Increased	Avoid nutrient deficiency/malnutrition[6-8]
Protein	Increased	Satiety, maintenance of lean body mass[9-11]
Fiber	Increased (+/-)	Satiety (pet-dependent)[12,13]
Moisture content	Increased (+/-)	Satiety/behavioral (pet-dependent)[14]
Calorie content (volume and weight basis)	Reduced	Behavioral (pet- and owner-dependent)[15,16,17]

guidance for minimum protein levels and other dietary factors are available.[1]

Strategies for success: Studies support the impact of fiber and moisture content, but this may not be applicable for each pet. For example, some cats may have strong individual preferences for either canned or dry food. Likewise, some families may have work schedules that do not allow for multiple trips outside for their dogs to defecate due to increased stool production on higher fiber diets.

3. Selection of Appropriate Diet and Treat Options

Evidence-based medicine can help guide recommendations for specific diets, supplements, treats, or other products with health claims for weight management. When a therapeutic diet or supplement is recommended, a conversation surrounding how that product was produced and what specific outcomes are expected by using the product can help families understand the rationale behind evidence-based medicine. The more information that is available, the more informed a decision can be when selecting diets. For example, some diets have been evaluated in clinical trials using either research colony animals or companion animals in home settings. When this product research is then published in peer-reviewed journals, it allows veterinarians to consider how the product was used (e.g., was this diet the only thing fed? What was the duration of feeding?), in what population of animals (e.g., was it only fed to healthy pets? Or was it also fed to obese and/or overweight animals?), and the expected outcomes (e.g., did this impact rate of weight loss or labwork values?). More detailed information on selecting specific diets for weight management can be found elsewhere.[3]

Strategies for success: Adherence may be increased by allowing treats, but reserve no more than 10% of the total desired daily calories for unbalanced foods. Asking about the relationship between the pet and all members of the household may uncover 'non-negotiable' aspects of the human–animal bond that can be discussed and included in the plan to increase adherence. Getting creative with substitutions for non-negotiables can also support adherence. Example questions such as 'Is there anything you feel strongly about including in the plan?' or 'Could you describe your daily routine with your pet?' can help veterinarians develop a plan both the owners and healthcare team feel comfortable with.

4. Creating an Initial Calorie Goal

If current intake can be accurately estimated, calories can be restricted to 80% of current intake to encourage weight loss. Recommendations for initial caloric restriction when current intake is unknown vary, but feeding 80% of resting energy requirements (70 x body weight (kg)$^{0.75}$) based on target weight can be effective and well tolerated.[1] Target weight is often used to determine calorie intake for weight loss; however, current weight can be used if target weight is difficult to determine or if there is concern for drastic restriction leading to nutrient deficiencies or unwanted begging behaviors. Regardless of starting point, the most important consideration is that pets receive follow up and the plan is adjusted as needed. As noted above, 10% of the total calories can be reserved for treats or other food items, particularly those that are integral to the human–animal bond.

Strategies for success: In situations of overfeeding or when the current intake is unknown, the initial calculated calorie goal may require a drastic change from current intake and feeding behaviors. For families in an earlier stage of readiness to change, this transition may be more successful when broken into smaller gradual changes. For example, if a cat is being fed ad libitum, an initial goal may be to transition to meal feeding first by gradually reducing the amount of time food is made available. This allows current intake to be better estimated at each mealtime and enables a smoother transition to the weight loss plan.

5. Monitoring and Adjustment of Goals

Calorie intake can be adjusted up or down in 10% increments at each check-in until the goal rate of body weight loss per week is reached. Ideally, pets will lose weight at a rate of 0.5%–2% of body weight per week.[1,2] A more gradual rate of weight loss for dog and cats with co-morbidities is safer and more realistic. Though pets can safely lose up to 2% of their body weight per week, the average (practical) rate of weight loss in one study at an obesity clinic was 0.6% body weight per week.[17] Once ideal weight has been reached, the majority of cats and dogs will continue to need calorie restriction and a low caloric density diet to prevent weight regain.[18]

COMMUNICATION TIP

One approach to discussing weight loss with a pet's owner is to shift conversations to quality of life and health-related outcomes to avoid defensiveness that can occur with labels such as 'fat' or 'obese.'

Strategies for success: If weight loss plateaus or reverses, revisiting a full nutritional assessment can identify opportunities for change. For example, measuring food by volume (i.e., cups or scoops) led to overestimating calorie intake by up to 152% in one study (Coe et al, 2019).[19] Especially for small dogs and cats or for those only needing smaller reductions in calorie intake, measuring food by weight and using kcal per gram to calculate target intake can reduce frustration among families struggling with plans that require fractions such as 2/5 or 3/8 of a cup of kibble.

6. Behavioral Management and Troubleshooting

Troubleshooting and supporting families when they encounter setbacks is an integral component of long-term weight management. There are many resources available for the veterinary team with troubleshooting guides for the most common challenges in weight loss programs.[1] Many of these behavioral management strategies provide solutions through opportunities for physical and mental enrichment to proactively address possible challenges. Exercise can be helpful, but it should be noted exercise alone is highly unlikely to cause significant weight loss. Brisk walks over increasing distances and swimming can be great activities for dogs, while food dispensing toys, hiding kibble around a room, and toys or laser pointers can be great ways to promote activity in cats.

Strategies for success: Proactive engagement with families can identify preferences for the family and the pet, such as asking what the pet's favorite activities are and incorporating them into the plan. Families may misinterpret begging behaviors as hunger when it is actually attention and interaction that their pets are seeking. Providing opportunities for quality time and interaction between families and their pets can redirect undesired behaviors into healthy physical and mental enrichment. Resources with creative strategies for including enrichment include the Indoor Pet Initiative (https://indoorpet.osu.edu/home).

COMMUNICATION STRATEGIES FOR SUCCESS: FOCUSING ON QUALITY OF LIFE

When families show resistance to change more than readiness to change, one approach is to shift conversations to quality of life and health-related outcomes to avoid defensiveness that can occur with labels such as 'fat' or 'obese.' For example, instead of focusing on 'obesity' being a diagnosis that requires treatment, you may be able to identify 'not being able to jump off the couch' as a specific measurable quality of life deficit with treatment focusing on movement without pain or hesitation. This allows conversations to focus on what families can do to make their pet happier and enjoy their time together more (without fear of

Table 2. Example conversation starters that focus on quality of life and health-related outcomes

Instead of:	Try:
Your cat's obesity is why her hair coat is so matted; she needs to lose weight to fix this. She'll groom again once she's thinner.	Let's brainstorm a plan your cat will enjoy and will facilitate her ability to meet her needs like grooming. We can monitor how often she grooms and how much easier it is for her as we go.
It's called 'tough love.' I understand it isn't easy, but you have to just tell your cat 'no' when they beg or they'll always be fat.	Your cat might be looking for food, or she could be looking for interaction with you. Instead of putting food or treats in her bowl when she is seeking your attention, let's brainstorm a few ideas to try, such as puzzle toys, play, brushing, or laser pointers.

judgement!). Example communication tactics can be found in **Table 2**, and there is additional information on communication in the chapter Communicating With Clients About Nutrition to Promote Compliance.

SUMMARY

While it is tempting to consider overweight and obesity a medical disease that is addressed by simply counting calories, long term success in weight management often requires a more comprehensive intervention with families. Understanding each family's unique human–animal bond can guide creation and implementation of more tailored weight management plans to set them up for success. These plans serve to support versus threaten the bond each family has with their pet. Comprehensive plans allow the veterinary care team to engage families where they are at and then empower families with tools and knowledge needed to provide the happiest and healthiest lives for their pets.

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RESOURCES

2021 AAHA Weight Management and Nutrition Guidelines for Dogs and Cats:
https://www.aaha.org/aaha-guidelines/2021-aaha-nutrition-and-weight-management-guidelines/home/

Helpful Tips:
-Algorithms and flowcharts for getting a diet history and performing a nutritional assessment
-Conversation starters and example phrases

2014 AAHA Weight Management Guidelines for Dogs and Cats:
https://www.aaha.org/aaha-guidelines/weight-management-configuration/abstract/

Helpful Tips:
-Step by step guide for creating a weight loss plan
-Troubleshooting guide for the most common challenges in weight loss programs

World Small Animal Veterinary Association Global Nutrition Guidelines:
https://wsava.org/global-guidelines/global-nutrition-guidelines/

Helpful Tips:
-Handouts for pet owners on how to pick high quality pet foods
-Non-branded body condition score and muscle condition score charts
-Listing of vetted websites with trusted pet nutrition information

CentreSquare:
https://www.purinainstitute.com/centresquare

Helpful Tips:
-Information on assessment of obese patients
-Energy requirement calculator for dogs and cats

Indoor Pet Initiative:
https://indoorpet.osu.edu/

Helpful tips:
-Information on cat and dog behavior including a problem-solving section
-Strategies for enrichment

Tufts Clinical Nutrition Service Petfoodology Website:
https://vetnutrition.tufts.edu/petfoodology/

Helpful Tips:
-University website created by board-certified veterinary nutritionists with frequently updated blogs on pet nutrition
-Multiple blogs on how to assess if a pet is overweight and the consequences of excess weight
-Extensive low calorie treat list that can be sent or printed for families

DIABETES MELLITUS IN DOGS

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KEY TAKEAWAYS

- The soluble carbohydrate content of the diet is a major determinant of the glycemic response to dog foods. A low to moderate carbohydrate diet can be beneficial depending on the insulin used and the individual response of the dog, and meals should have consistent carbohydrate content. The presence of concurrent conditions such as pancreatitis may make selection of a low to moderate carbohydrate diet difficult.
- The traditional management regimen involves twice-daily administration of an intermediate-acting insulin matched with twice-daily feeding of consistent meals. This approach typically works well in dogs with uncomplicated diabetes, but not for dogs with an unreliable appetite. Feeding management, particularly a consistent schedule, is important for dogs treated with twice-daily insulin.
- An important advantage of using a long-acting, basal insulin treatment protocol for canine diabetes is that for most dogs there is no requirement to match feeding with the timing of insulin injections. Nutritional management, including diet and feeding management, may potentially improve glycemic control in dogs treated with basal insulin.

DEFINITION AND DIAGNOSIS

Diabetes mellitus is defined by project ALIVE (Agreeing Language In Veterinary Endocrinology) as "a heterogeneous group of diseases with multiple etiologies characterized by hyperglycemia resulting from inadequate insulin secretion, inadequate insulin action, or both."[1] This results in altered carbohydrate, fat, and protein metabolism, which manifests as hyperglycemia, hyperlipidemia, polyuria, lethargy, weight loss, polyphagia, and reduced immunity.

Diagnosis of diabetes mellitus in dogs is usually based on the presence of persistent hyperglycemia along with clinical signs, especially polyuria, polydipsia, weight loss, and polyphagia.[1]

INSULIN PHYSIOLOGY IN DOGS

Ideally, management of diabetes in dogs should aim to mimic normal physiology as much as may be practically achieved. In healthy dogs, insulin synthesis and secretion are stimulated predominantly by increases in blood glucose concentrations. Endogenous insulin secretion can be divided into two phases:

- The basal phase, in which insulin is secreted continuously at a relatively constant rate.[2] Basal insulin secretion limits hepatic glucose production and lipolysis in the fasting state. Although basal insulin secretion is relatively constant throughout the day, it increases when insulin resistance develops (for example, with obesity, Cushing's syndrome, or diestrus).[3]
- The endogenous bolus phase, in which insulin is secreted in response to nutrients digested and absorbed from the gut. Endogenous bolus insulin production primarily suppresses hepatic glucose output and stimulates glucose utilization by muscle and adipose tissue during the postprandial period, thus curbing hyperglycemia after meals.[2] Endogenous bolus insulin secretion is largely determined by factors such as the quantity of food consumed, the carbohydrate, fat, and protein contents of the meal, carbohydrate source, gastrointestinal transit time, and the effects of incretin hormones.[2,4] Thus, in healthy dogs, endogenous bolus insulin production varies significantly in shape and magnitude with diet. Insulin increases within minutes after feeding and often peaks within 30 minutes at 5–7 times the baseline concentration. It can remain increased for 6–9 hours in dogs depending on the diet and amount fed.[5-8]

COMMON COMPLICATING FACTORS OF CANINE DIABETES

There are several complicating factors that make management of diabetes mellitus in dogs more difficult (**Box 1**):

- Entire female dogs typically present with diabetes during the insulin-resistant diestrus phase of their reproductive cycle.[9] Prompt insulin treatment combined with either ovariohysterectomy or spontaneous end of diestrus has been reported to achieve diabetic remission in about 10% of cases.[10]
- In populations where neutering of young dogs is routine, the most common concurrent conditions in diabetic dogs are Cushing's syndrome and pancreatitis.[11] Bacteriuria is also commonly reported, although its pathological significance can be difficult to interpret in diabetic dogs with polyuria.
- The most pronounced effects of Cushing's syndrome on glucose metabolism in dogs are insulin resistance, excessive postprandial hyperglycemia, perceived short duration of insulin action, and/or substantial within-day and/or day-to-day glycemic variability.[12]
- The effects of pancreatitis on glucose metabolism are very variable and include reduced food intake due to inappetence/anorexia, transient or permanent loss of beta cell function, insulin resistance when there is severe inflammation and pain, and, in some cases of chronic pancreatitis, progression to exocrine pancreatic insufficiency (EPI).
- Obesity causes insulin resistance in dogs as it does in all species, with the degree of insulin resistance positively correlated with the severity of adiposity.[13] However, type 2 diabetes mellitus, a condition strongly associated with obesity in people and cats, is not recognized in dogs. While diabetic dogs can develop insulin resistance, they are always insulin-dependent.
- Disease processes that cause progressive loss of beta cells, such as immune-mediated destruction or chronic pancreatitis, will limit the capacity of obese dogs to compensate for obesity-associated insulin resistance. This might result in earlier presentation with diabetes than if the dog was lean.
- Obesity and other causes of insulin resistance have an additive effect on insulin requirements and the risk of progression to clinical diabetes in dogs. Dogs with Cushing's syndrome had greater risk for developing diabetes if they were entire females and/or were overweight or obese on initial presentation.[14] The same cumulative insulin resistance occurs in obese female dogs in diestrus.[15]
- Changes in body weight and body condition score can affect insulin resistance and the dog's required insulin dose.

COMMUNICATION TIP

Many owners will not report diet changes to the veterinary team, especially those relating to feeding of treats. Therefore, a comprehensive diet history should be obtained at each reassessment, and owners should be encouraged to keep a food diary.

KEY NUTRIENTS FOR MANAGEMENT OF DIABETES IN DOGS

The soluble carbohydrate content of the diet is a major determinant of the glycemic response to food, and so a low to moderate carbohydrate-restricted commercial dog food can be beneficial for diabetic dogs. Other factors that impact glycemic response include the insulin used and the response of the individual dog to food consumption. Meals should have consistent carbohydrate content. The presence of concurrent conditions may affect a clinician's ability to select a low carbohydrate diet. The guaranteed or typical analysis statements on pet foods do not provide information on the carbohydrate content of the food, and so this must be obtained from the manufacturer. Low glycemic index carbohydrate sources that also elicit low postprandial insulin responses in healthy dogs are likely preferable.[4]

Although several studies indicate that high-fiber diets, compared with low-fiber diets, might be associated with improved glycemic control, there has been no clear demonstration of clinical benefit for diabetic dogs of feeding a high-fiber, moderate carbohydrate formulation compared with feeding an

Box 1. Potential challenges in the medical and nutritional management of diabetic dogs

- **Anorexia/hyporexia** – This typically indicates that concurrent illness might be present, and so prompt veterinary assessment is recommended. A trend to reduced appetite might also be associated with resolution of polyphagia indicating improvement in response to treatment.
- **Increases or decreases in dietary carbohydrate concentration or other diet change** – This is especially a problem when owners do not report diet changes to the veterinary team. It is recommended that a comprehensive diet history is obtained at each reassessment. Owners should also be encouraged to keep a food diary.
- **Feeding schedule changes** – This is especially important for dogs treated with twice-daily administration of intermediate-acting insulin.
- **Treat administration** – Treats such as dental chews that typically have a relatively high digestible starch content can affect glycemic control. Many owners will not volunteer information about treat feeding unless specifically questioned about this. The timing of treats may also affect glycemic control for dogs on intermediate-acting insulin.
- **Insulin dosing errors** – This must be considered whenever there is an unexplained change in diabetic control, even for owners who are experienced with insulin administration.
- **Changes in body weight and body condition** – Body weight, body condition score, and muscle condition score should be recorded at each reassessment. Improvement of diabetic control is typically associated with weight gain. It might then be necessary to reduce calorie intake to avoid unwanted weight gain. A reduction in food intake might necessitate decrease of the insulin dose.
- **Insulin resistance** – The most common causes of insulin resistance are diestrus in entire female dogs, and Cushing's syndrome and obesity in all dogs.
- **Concurrent disease** – Especially those that require dietary fat restriction and so limit the option of feeding a low to moderate carbohydrate diet (for example, pancreatitis, hyperlipidemia).
- **Vigorous or prolonged exercise** – For example, running beside a person riding a bicycle or working with livestock. Note that routine daily exercise walking on a lead or off-lead play at a dog park usually has minimal impact on diabetic control.

adult maintenance diet with moderate fiber content but low carbohydrate content.[7,16] Dietary fat restriction is recommended for diabetic dogs with concurrent chronic pancreatitis or persistent hypertriglyceridemia. Nutrient requirements for concurrent diseases usually have priority over those for diabetes mellitus.

Most well-managed diabetic dogs require a similar amount of food per day as healthy non-diabetic dogs of similar age, gender, and lifestyle. Dogs with suboptimal diabetic control usually need to consume more calories than their calculated maintenance requirement to compensate for a tendency to lose weight. In the authors' experience, diabetic dogs with reduced exocrine pancreatic function have increased caloric requirement compared with healthy dogs.

DIET OPTIONS FOR DIABETIC DOGS

Diabetic dogs are more likely to readily accept a diet that has a formulation similar to the diet they were consuming before diagnosis of diabetes. Diets formulated for canine adult maintenance with moderate dietary fiber and carbohydrate content will be suitable for most diabetic dogs. If a dry diet is preferred, a veterinary therapeutic diet specifically formulated for management of diabetes may be the most appropriate option, provided no other health issues necessitating dietary modification are present. Wet commercial canine diets often have lower carbohydrate content versus dry diets, but manufacturers should be contacted for the typical analysis that includes carbohydrate content. Wet food may be cost-prohibitive for owners, especially when feeding large dogs.

In some cases, better glycemic control may be achieved with a diet with lower carbohydrate content. To identify a suitable commercial wet diet, it is necessary to 1) check the product label for a nutritional adequacy statement for the appropriate life stage, and 2) obtain the specific dietary carbohydrate content on a dry matter or calorie basis of the product from the manufacturer (this information might be on the product label, on the product website, or obtained by direct communication with the manufacturer). An alternative approach is to use a home-cooked diet specifically formulated for the individual patient. With consultation of a board-certified veterinary nutritionist, a customized complete and balanced home-cooked diet with lower carbohydrate content may be trialed to see if glycemic control is improved compared with a moderate or higher carbohydrate diet.

A fat-restricted diet should be considered for diabetic dogs with concurrent chronic pancreatitis or persistent hypertriglyceridemia. High-fiber, restricted-fat diets should not be routinely recommended for diabetic dogs with thin body condition.

THE IMPORTANCE OF FEEDING MANAGEMENT/SCHEDULES FOR DOGS TREATED WITH INSULIN

Exogenous insulin therapy is the mainstay of clinical management of diabetes mellitus in dogs, and the primary goals are long-term resolution of all clinical signs and avoidance of insulin-induced hypoglycemia. A successfully managed diabetic dog will have no polyphagia, lethargy, or polydipsia, and will be able to maintain body weight.

Treatment with an Intermediate-Acting Insulin such as Lente, NPH, PZI, Glargine U100, or Detemir

The traditional management regimen involves twice-daily administration of an intermediate-acting insulin, such as lente, NPH, PZI, glargine U100, or detemir, matched with twice-daily feeding of consistent meals. This approach typically works well in dogs with uncomplicated diabetes but works less well for dogs with an unreliable or finicky appetite. To avoid hypoglycemia, it is frequently recommended to administer the intermediate-acting insulin only after a full meal has been consumed, which can result in a lot of anxiety for owners of dogs that have a finicky appetite. It is also typically recommended to administer half the usual dose of insulin when a diabetic dog does not eat any of the accompanying meal.

Meals should be highly palatable so that food intake is predictable. Dogs with a reliable appetite may be fed immediately following the insulin injection so that the meals are given as a reward for complying with the injections. The majority of diabetic dogs will readily consume meals twice daily following the insulin injections if the meals are highly palatable and contain half the daily caloric requirement. For finicky eaters, the meal should be fed at the time of insulin administration and remain available until the expected end of the period of maximal exogenous insulin activity. Owners can try tactics such as warming or handfeeding to encourage food intake. In some cases, adding a safe palatability enhancer such as warmed chicken broth with no onions or garlic can be beneficial.

Treatment with a Long-Acting, Basal Insulin such as Glargine U300 or Degludec

Treatment of canine diabetes with a basal insulin, such as glargine U300 or degludec, offers several advantages including a more flexible and convenient daily routine for the dog's owner.[8,17] An important difference from the traditional regimen used with intermediate-acting insulin products is that for most dogs there is no requirement to match feeding with insulin injections. Feeding management differences between diabetic dogs treated with intermediate-acting versus basal insulin are shown in **Table 1**.

A basal insulin is administered irrespective of food administration. Blood glucose is then expected to rise following the meals and decline back to baseline when digestion and absorption have subsided (**Figure 1**). The observed blood glucose fluctuations depend on the type of food and the frequency of feeding. This means that glycemic control may be improved by changing the timing of the meals, the relative portion sizes fed at mealtimes, the frequency of meal feeding, and/or by reducing the carbohydrate content of the meal(s).[17]

Unlike the traditional approach of using an intermediate-acting insulin, there is often no need to reduce the dose of basal insulin because of planned or unplanned fasting, and there is minimal risk of hypoglycemia if the dog has vomited food after eating.

Table 1. Feeding management strategies for dogs on intermediate-acting versus long-acting basal insulin

Treatment with twice-daily administration of an intermediate-acting insulin such as lente, NPH, PZI, glargine U100, or detemir	Treatment with once- or twice-daily basal insulin such as glargine U300 or degludec
There is an exogenous insulin peak that ideally should be matched to the postprandial period	It is typically not necessary to match insulin action with the postprandial period
Twice-daily feeding of consistent meals at the times of insulin administration is typically recommended	Meal consumption is not necessary at the time of injections
The twice-daily feeding schedule works well for dogs with a reliable appetite, but can be stressful for owners of dogs with an unreliable appetite	There is more flexibility regarding the daily feeding schedule, which means more convenience and less stress for many owners, especially when the dog has a finicky or unreliable appetite
Treats or snacks should be consumed soon after mealtimes	Treats or snacks may be fed at times different than mealtimes
Glycemic control may be improved by reducing the carbohydrate content of the meals	Glycemic control may be improved by changing the timing of the meals, the relative portion sizes fed at mealtimes, the frequency of meal feeding, and/or by reducing the carbohydrate content of the meal(s)
A lower insulin dose is typically recommended when the dog is fasted	There is often no need to reduce the dose of insulin when the dog is fasted

However, it is prudent to monitor blood glucose in this scenario.

In most dogs, good control of clinical signs is achieved when using a basal insulin alone. In a small minority, a bolus of an intermediate-acting insulin at the time of at least one meal per day may be needed in order to optimize glycemic control.[17,18]

MANAGEMENT OF HYPOGLYCEMIA

If mild signs of hypoglycemia develop, the owner should feed a meal of the dog's usual food or high-carbohydrate treats. Handfeeding might be necessary to encourage the dog to eat. If the dog is unwilling or unable to eat, honey or syrup containing a high glucose concentration can be administered orally. Suitable syrups are marketed for use by human diabetics and should be kept in reserve by all owners of diabetic dogs. When the dog recovers, a meal of the dog's usual food should be fed immediately, and then the owner should contact their veterinarian before administering another insulin dose.

TREATS AND SNACKS

If treats or snacks are fed, they should be consumed close to mealtimes for dogs treated with intermediate-acting insulin. This is especially the case for foods such as dental chews that typically have a relatively high digestible starch content. Much more flexibility is permissible with the timing of treat and snack feeding in dogs treated with basal insulin. Treats containing high sugar or fat should be avoided.

Vigorous or prolonged exercise can be associated with increased risk of hypoglycemia in insulin-treated diabetic dogs. This can be managed with feeding of snacks prior to and during exercise. Management strategies during exercise must be individualized for each dog.

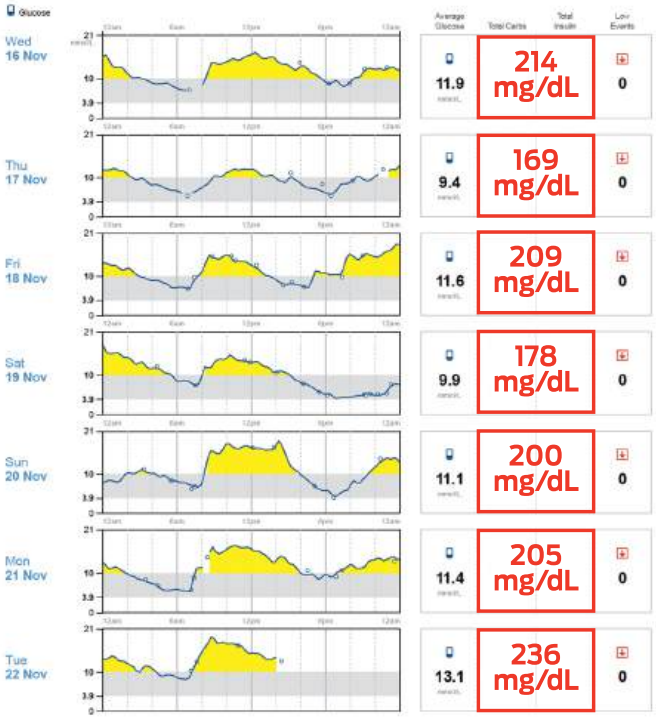
MONITORING

One of the key clinical signs of untreated diabetes mellitus is loss of body weight and condition, despite polyphagia. With institution of appropriate medical and nutritional therapy, weight loss is usually arrested before optimal glycemic control is achieved. It is, therefore, important to monitor body weight, body condition score, and muscle condition score at each re-assessment to track changes. Glycemic monitoring is used to evaluate response to the insulin and dietary regimen. Serum triglyceride concentration can be monitored to identify persistent hypertriglyceridemia,

Figure 1. The effect of feeding in a diabetic dog treated with a long-acting basal insulin

24-hour glucose data using a continuous glucose monitor in a diabetic dog. The x-axis shows time, and the y-axis shows blood/interstitial glucose concentrations. Identical meals were fed at 7:00 am and 6:00 pm. Average daily interstitial glucose results are provided in the right panel, showing good glucose control.

In dogs treated with basal insulin, blood glucose increases following the meals and declines back to baseline when digestion and absorption are complete. Note that the typical postprandial hyperglycemic period in dogs is 6-9 hours. The result is a glucose curve with an inverse shape to the typical U-shaped glucose curve that is expected (but not always achieved) in dogs treated with twice-daily intermediate-acting insulin. Note that there is day-to-day variability of postprandial increases in glucose following food consumption.



and to monitor the response to feeding a fat-restricted diet. Exogenous insulin therapy will result in resolution of hypertriglyceridemia in some diabetic dogs, while others require dietary fat restriction in addition to insulin therapy.

CONCLUSION

Overall, diet selection and feeding management should be individualized for each diabetic dog. In general, a complete and balanced diet with low to moderate carbohydrate concentration can be beneficial for diabetic dogs, but the nutritional assessment, including body condition score, muscle condition score, and diet history, will impact the feeding plan. Other factors that will impact diet selection and feeding management include the presence of concurrent conditions such as pancreatitis or hypertriglyceridemia, and the type of insulin used. Client communication is also an important component of developing a feeding plan for a diabetic patient.

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DIABETES MELLITUS IN CATS

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KEY TAKEAWAYS

- Remission is a main therapeutic goal in newly diagnosed diabetic cats because it increases the quality of life of both the cat and owner, and survival is increased compared with cats who do not achieve remission.
- The probability of remission is optimized by early institution of long-acting insulin, a low-carbohydrate diet, frequent glucose monitoring, and appropriate insulin dose adjustments aimed at achieving normal or near normal blood glucose concentrations for most of the day.
- Simpler protocols that achieve less rigorous glycemic control are appropriate for clients who would otherwise euthanize their cat.
- In long-term diabetics and cats with comorbidities that reduce survival, supporting the cat's owner to cope with ongoing management, resolving clinical signs of diabetes, and managing comorbidities takes precedence.

KEY DIAGNOSTIC TOOLS AND MEASURES

Persistent hyperglycemia is termed *diabetes mellitus*, and results from insufficient insulin secretion from pancreatic beta cells to maintain blood glucose concentrations in the normal range. Peripheral insulin resistance is typically a contributing factor, as is advancing age.

Documentation of persistent hyperglycemia ≥ 180 mg/dL (≥ 10 mmol/L) is required for diagnosis. Concurrent clinical signs of polyuria, polydipsia, and a history of weight loss are common and supportive, but alone, are not diagnostic of diabetes. Glucosuria may help confirm the diagnosis, but may not occur until blood glucose is approximately 250–290 mg/dL (14–16 mmol/L).[1,2] If blood glucose concentration is only moderately elevated (180–300 mg/dL; 10–17 mmol/L), transient stress hyperglycemia needs to be differentiated from persistent hyperglycemia of diabetes. In these cats, diagnosis of diabetes should be based on increased glycated hemoglobin (HbA1c), or two to three successive blood samples taken at least 4 hours apart in a non-stressful environment, or with a continuous (flash) glucose monitor at home. Fructosamine is not a sensitive diagnostic tool if blood glucose is < 360 mg/dL (< 20 mmol/L). Additional clinical signs can also include muscle wasting and peripheral neuropathy resulting in weakness when walking or jumping.

PATHOPHYSIOLOGY

More than 80% of diabetic cats are thought to have type 2 diabetes mellitus which results from beta cell failure in the presence of insulin resistance.[3] The exact mechanisms for beta cell failure are multifactorial and not fully understood. The remaining cases of feline diabetes are associated with other specific types of diabetes. The most common cause is hypersomatotropism (acromegaly) resulting in marked insulin resistance. Other less common causes include hyperadrenocorticism resulting in insulin resistance, or pancreatic adenocarcinoma or pancreatitis resulting in pancreatic destruction. Once blood glucose increases, the associated disturbances in intracellular beta cell metabolism further suppress insulin secretion and damage beta cells (often termed *glucotoxicity*). With early institution of appropriate insulin therapy, this suppression of insulin secretion is reversible, but over time, chronic hyperglycemia leads to loss of beta cells.[4,5]

Most cats are insulin dependent at the time of diagnosis because endogenous insulin is minimal as a result of reversible suppression of insulin secretion or because of irreversible loss of beta cells. Depending on the underlying cause and duration of diabetes and

management, 20–90% of diabetic cats are reported to achieve non-insulin dependence (termed *diabetic remission*). Diabetic cats are considered to be in remission if they maintain a normal (< 117 mg/dL; < 6.5 mmol/L) or near-normal (117 mg/dL to < 180 mg/dL; 6.5 mmol/L to < 10 mmol/L) blood glucose concentration (termed *impaired fasting glucose*) after withdrawal of insulin for at least 2–4 weeks.[6-8] Most cats in diabetic remission still have abnormal glucose metabolism, and 80% have impaired glucose tolerance predisposing them to relapse. In fact, 25–30% of cats relapse and redevelop diabetes within a year.[7,9]

COMMUNICATION TIP

"In many newly diagnosed diabetic cats, the priority for management is to achieve diabetic remission because of the increased quality of life advantages for the client and cat."

KEY FACTORS IN MANAGEMENT

A primary goal of treatment of diabetes in cats is to ensure that the owner feels supported and can easily cope with the requirements of treatment. Therefore, it is important to provide practical and flexible options that suit the individual owner and cat. In newly diagnosed diabetic cats without life-reducing comorbidities, where possible, the initial treatment goal should be to aim for diabetic remission. For some owners who might otherwise elect for euthanasia, a simpler approach that aims to resolve clinical signs while minimizing the risk of hypoglycemia might be more appropriate.

Three key factors optimize the probability of remission, and therefore longevity of a cat diagnosed with diabetes. These are:

1. Early initiation of treatment using a long-acting insulin (**Box 1**)
2. Low intake of dietary carbohydrate
3. Frequent blood or interstitial glucose monitoring and appropriate insulin dose adjustments to avoid clinical hypoglycemia and facilitate maintaining blood glucose concentrations (measured with a meter calibrated for feline blood or adjusted for the methodology used) throughout most of the day between 63 and 180 mg/dL (3.5 and 10 mmol/L) by 4–8 weeks of therapy.

For owners who are seeking a simpler approach, it might be more appropriate to aim for blood glucose concentrations to be mostly maintained below the renal threshold (< 270 mg/dL, < 15 mmol/L). However, there is a benefit of tighter glycemic control if remission is the goal.[10]

KEY NUTRIENT MODIFICATIONS

Diets low in soluble carbohydrate (CHO) or Nitrogen Free Extract (NFE) are considered beneficial for management of feline diabetes and facilitate achieving remission. By limiting dietary carbohydrates, blood glucose is maintained primarily from hepatic gluconeogenesis, and blood glucose fluctuations after a meal are minimized.[11] A low-CHO, high-protein diet helps facilitate achieving remission in newly diagnosed diabetic cats.[12] Most cats achieving diabetic remission have reduced capacity of the remaining beta cells to control blood glucose.[7] Therefore, minimizing the demand for insulin by feeding a low-carbohydrate diet is important before and after remission. For cats with other life-reducing comorbidities, a low-carbohydrate diet may not be appropriate when management of the comorbidity needs to take precedence.

THERAPEUTIC FEEDING PRINCIPLES

The management goals in newly diagnosed diabetic cats are to avoid insulin-induced clinical hypoglycemia and to optimize the chance of achieving remission by minimizing hyperglycemia. Low-carbohydrate diets are important to help achieve remission, which is most likely in the first 2–6 months after diagnosis, if managed with appropriate therapy.[6,9,12,13] Achieving diabetic remission increases survival and enhances the quality of life of the cat and owner.[14] Therefore, it is an important goal in many newly diagnosed diabetic cats. However, the probability of remission is low in cats that have been diabetic for more than one year, and resolving clinical signs while avoiding clinical hypoglycemia take precedence. Dietary management of other comorbidities must also be considered. In a newly diagnosed cat, a low-carbohydrate diet is recommended when appropriate and comorbidities

Box 1. An example of an insulin dosing protocol reported to achieve high remission rates in newly diagnosed diabetic cats[9] and advocated by one of the authors (JR). Less intensive protocols that provide more flexible options may be more appropriate for some cats and their owners.

Goals

In a newly diagnosed cat, if possible, aim for optimizing glucose concentrations while avoiding clinical hypoglycemia, because this increases the probability of remission compared with just controlling clinical signs.[10]

In a long-term diabetic cat or one with other life-reducing comorbidities, controlling clinical signs of diabetes and the comorbidity take precedence.

Monitoring

Glucose (blood or interstitial) is best monitored at home to minimize the confounding effect of stress hyperglycemia using either a continuous (flash) glucose monitor or a portable glucose meter, preferably one calibrated for feline blood. This is essential to determine the level of glycemic control and appropriate insulin dosage to facilitate achieving optimum glycemic control.

Phases of insulin dose adjustments aimed at achieving remission in a newly diagnosed diabetic cat

In general, there is a phase of gradual insulin dose adjustments every 3–7 days over 4–6 weeks, then a phase of holding that insulin dose for at least 2–4 weeks if nearly all blood glucose concentrations are between 63 and < 180 mg/dL (3.5 to < 10 mmol/L) during the day.

If this level of glycemic control is achieved, then the next phase is a gradual reduction of dose every 7–14 days to determine if the cat can maintain blood glucose in the target range on a lower dose of insulin, suggesting endogenous insulin secretion.

The dose decreases continue until a dose of 0.25–0.5 U twice daily is reached (use a 0.3-mL insulin syringe) or 1 U once daily for glargine (U300). Administration is then decreased to once daily for 2–4 weeks and then discontinued. If blood glucose is not maintained in the target range, insulin dose needs to be increased to a dose which will control blood glucose.

If the nadir (lowest) glucose concentration is in the normal range, but substantial periods of hyperglycemia > 180 mg/dL (10 mmol/L) are occurring, insulin type, frequency, and/or diet need adjusting.

Strategies if glucose (blood or interstitial) is in normal range when the next insulin dose is due

If glucose is in the normal range (63 to < 117 mg/dL; 3.5 to < 6.5 mmol/L) at the time of the next insulin injection (pre-insulin glucose concentration), try one of three options:

i. Feed the cat and wait 1–2 hours, and if blood glucose is above the normal range, give the regular dose; if not above normal range, reduce dose by 0.25–0.5 U (1 U glargine U300).

ii. Split dose and give most initially and remainder in 1–2 hours if blood glucose has increased > 117 mg/dL (≥ 6.5 mmol/L).

iii. Feed and reduce dose by 0.25–0.5 U (1 U glargine U300).

If blood glucose is consistently high 12 hours later when the next insulin dose is due with the three options, then administer the normal dose of insulin and monitor carefully for response. Peak insulin action when using glargine U100, U300, or detemir insulin is at least 2 hours and often 5–8 hours after administration, so for many cats the regular dose can be given even when pre-insulin glucose concentration is in the normal range.

Managing Hypoglycemia

Insulin dose is reduced at any point in the cat's management if glucose is < 54–63 mg/dL (< 3–3.5 mmol/L), or if clinical signs of hypoglycemia occur. If signs are mild (dilated pupils), trembling, or staggery gait, add glucose syrup or honey to the food and feed immediately. Marked signs including seizures are an emergency and clients should have a glucose syrup used for human diabetic patients to rub on the gums or give per rectum, and the cat transported to the veterinary clinic.

Cats already on insulin therapy and being changed to a low-carbohydrate diet should have insulin dose decreased initially by 30–50%, because hypoglycemia can develop with the reduced carbohydrate load.

should be managed in other ways when possible. However, cats with later stage CKD (IRIS Stage 3–4), for example, are not appropriate candidates for a low-carbohydrate diet due to the higher protein and phosphorus found in these diets. Dietary management of other comorbidities also takes greater priority in cats that are unlikely to achieve remission.

Low-CHO foods help minimize the demand on beta cells to secrete insulin and are associated with increased rates of remission in newly diagnosed diabetic cats and better glycemic control in all diabetic cats, compared with feeding higher carbohydrate foods, even if they contain higher fiber. For example, remission rates were 50% higher (68% versus 41%) when a low-carbohydrate, low-fiber diet was fed compared with a moderate-carbohydrate, high-fiber diet.[12] Achieving remission is optimized by frequent glucose monitoring and insulin dosing protocols aimed at achieving normal or near-normal blood glucose concentrations for most of the day, compared with protocol based purely on controlling clinical signs.[9,10,13]

It is usually recommended that diabetic cats be fed twice daily at the time of each insulin injection, although it is acceptable to provide smaller meals more frequently. When using glargine 300 U/mL, for many cats there is no advantage in timing of feeding and insulin administration to coincide. Inconsistent carbohydrate content or food consumption from day to day, for example, associated with a free choice feeding method, is not recommended because this might contribute to unwanted glycemic variability (**Figure 1**). Regardless of the frequency of feeding, it is critical that the daily energy fed is calculated to achieve or maintain an ideal body weight, while maintaining a low carbohydrate intake that does not vary day to day.

Overweight and obesity are associated with insulin resistance; therefore, maintaining or achieving an ideal body weight is important in facilitating and maintaining remission in diabetic cats. In one study, a 44% increase in body weight decreased insulin sensitivity by over 50%.[15] Overweight and obese diabetic cats should be fed restricted amounts of a nutrient-dense diet appropriate for management of their diabetes and weight loss. In many diabetic cats, remission occurs before significant weight loss. It is very important to continue nutritional management of body condition and carbohydrate consumption once remission is achieved, because rebound weight gain and/or changing to a high-carbohydrate diet will likely predispose to relapse of insulin-dependence.

- **Treats** – High-CHO treats should be avoided, and consumption of low-CHO treats limited to less than 10% of total daily calories.
- **Tips for increasing palatability** – When changing a cat to a new diet, appetite issues can be a concern. The diet transition should only be introduced when the cat is eating well in the home environment, and pathological weight loss has been arrested. Transition the diet change from the regular diet to the suitable diabetic diet over 5–14 days; a longer period may be needed for cats that are more resistant to change. Feeding canned food may increase palatability for some cats.
- **Energy** – Many obese cats achieve remission before substantial weight loss occurs and before an ideal weight is reached; however, it is critically important that the amount of energy fed supports continued weight loss until ideal weight is reached, to reduce demand on beta cells. Increasing dietary water and meal volume can assist with weight management in cats, slowing consumption of food, increasing the owner's perception that more food is being offered and may help increase satiety.[16] Examples of ways to increase dietary water and meal volume include feeding wet food or adding cooked zucchini at less than 10% of total daily calories.

CLIENT EDUCATION POINTS

- Depending on the insulin used and diet, meals may or may not need to be timed to coincide with insulin administration. Typically, cats are fed at the time of insulin injection at 12-hour intervals when using insulin twice daily. A complete and balanced commercial feline diet should be fed, but the actual amount of dietary carbohydrate needs to be confirmed by the veterinarian or manufacturer. Homemade diets that are ultra-low in carbohydrate are high in phosphorus and are frequently not complete and balanced unless formulated by a board-certified veterinary nutritionist.
- Cats can become non-insulin dependent (diabetic remission); therefore, close monitoring is essential. It is essential to continue feeding a low-CHO diet to cats in remission to minimize demand on beta cells to secrete insulin. If comorbidities are present,

Figure 1 A & B. Changes in glucose variability in a diabetic cat over 3 months

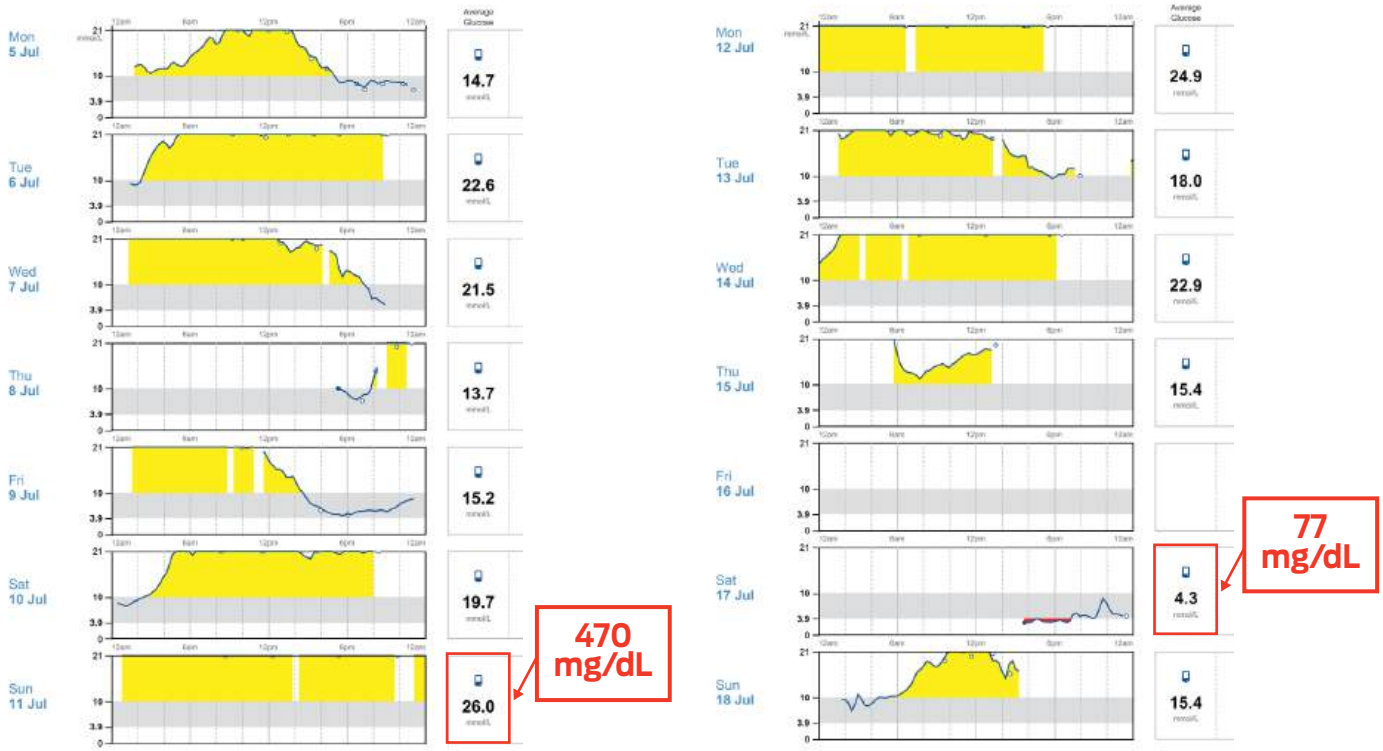

Figure 1A. Interstitial glucose concentrations measured by a Freestyle Libre continuous glucose monitor in an 11-year-old, neutered male, Burmese cat fed a low-carbohydrate, wet cat food twice daily at 8:00 am and 8:00 pm and with access to a dry cat food throughout the day. Current insulin treatment: 8 units glargine U300 BID. Body weight 6.2 kg; body condition score 6.5/9.

Note the frequent hyperglycemia and excessive day-to-day glycemic variability with average interstitial glucose ranging from 77 to 470 mg/dL (4.3-26.0 mmol/L).

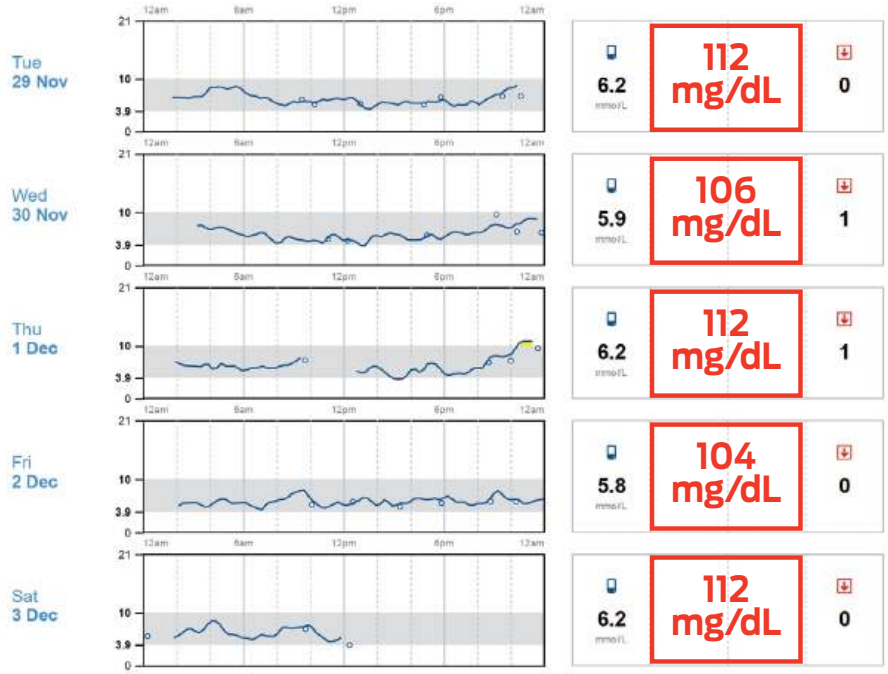

Figure 1B. Interstitial glucose concentrations from the same cat 3 months later showing markedly reduced glucose variability. Access to dry cat food was stopped and only low-carbohydrate, wet cat food was fed. Insulin requirement decreased by 50% so that the insulin dose needed to be progressively decreased in a stepwise manner. Body weight 6.1 kg; body condition score 6.5/9. Current insulin treatment: 4 units glargine U300 BID. Average daily interstitial glucose ranged from 104–112 mg/dL (5.8–6.2 mmol/L).

efforts should be made to choose an appropriate diet that is still low in dietary carbohydrate.

- It is important for owners to be prepared for hypoglycemic episodes in case they occur.[17] Reduced ingestion of food or subsequent vomiting of a meal after insulin administration is commonly reported in cats with clinical hypoglycemia at an emergency center. These signs might be either a consequence or a cause of insulin-induced hypoglycemia. Therefore, it is crucial that food intake be reliable and predictable to minimize the risk of insulin-induced hypoglycemia. Cats with mild to moderate signs of hypoglycemia, such as weakness, trembling, and unsteadiness, that are still able to eat should be immediately fed honey or glucose syrup mixed with cat food. Cats cannot taste sweet foods and appear not to notice if honey or glucose syrup is thoroughly mixed with the food.[18] If signs are severe such as seizure or coma, glucose syrup designed for human diabetic patients can be applied to the gums. No more insulin should be administered until veterinary advice is obtained.

TREATMENT

There is a substantial (10%) risk of euthanasia when a pet is diagnosed with diabetes, and a further 10% are euthanized in the first 12 months of treatment.[19] Risk factors for clients electing for euthanasia of their diabetic pet include presence of concurrent disease, cost of treatment, age of pet, problems obtaining adequate control, concerns about pet welfare, and impact on owner's lifestyle.[19] Factors impacting on the owner's quality of life were insufficient control in their pet's diabetic management, difficulties leaving their pet for a holiday, and worry about hypoglycemia.[20] These need to be considered in conversations with the client about the management of their diabetic cat, and clinicians should be prepared to offer flexible, practical, and individualized options.

Long-acting insulins such as glargine 100 U/mL (U100) and detemir dosed twice daily are reported to be associated with the highest probability of remission when combined with a low-CHO diet to control blood glucose concentrations.[6,9,13] Glargine 300 U/mL (U300) is a long-acting insulin in cats with a similar duration of action to glargine U100 (16.8 hour versus 13.4 hour) and less variability,[21] and in some cats good glycemic control can be obtained with once-a-day administration.

If the goal is to achieve diabetic remission, then a treatment and monitoring approach is required that aims to achieve normal or near normal blood glucose concentrations (63 to < 180 mg/dL; 3.5 to < 10 mmol/L) for all or most of the day. Remission is more readily achieved using an intensive glucose monitoring protocol.[10] The owner needs to be made aware that longevity is increased in cats that achieve remission, and that a protocol based purely on controlling clinical signs will likely achieve suboptimal glycemic control and decrease the probability of remission and decrease survival.[10,14] An insulin dosing protocol aimed at achieving diabetic remission in newly diagnosed cats is shown in **Box 1**.

MONITORING

In newly diagnosed cats, blood glucose concentrations (or surrogates measures such as interstitial glucose and urine glucose) need to be monitored to determine the level of glycemic control and appropriate insulin dosage, with the aim of maintaining as close to a normal blood glucose concentration as possible while avoiding hypoglycemia. Blood and/or interstitial glucose are best monitored at home to minimize the confounding effect of stress hyperglycemia using either a continuous (flash) glucose monitor or a portable glucose meter, preferably one calibrated for feline blood.

Alternatively, or in addition, urine glucose monitoring may be performed daily when the cat is treated with insulin with the goal of decreasing the insulin dose when urine consistently tests negative for glucose for 1–2 weeks. However, clients should be aware that glycemic control will likely be suboptimal in the critical 16 weeks following diagnosis if urine glucose concentration is the sole monitoring tool, and therefore may reduce the probability of remission.

For early detection of relapse, cats in remission should have blood glucose measured weekly, and insulin reinstituted if blood or interstitial glucose is > 180 mg/dL (10 mmol/L). Routine glucose monitoring is recommended to facilitate early detection of diabetic relapse (blood glucose > 10 mmol/L or 180 mg/dL). Prompt reinstitution of insulin is recommended, because delay until reappearance of clinical signs likely reduces the probability of achieving a second remission. Once weekly urine glucose monitoring with the goal of reinstituting insulin treatment if urine tests positive for glucose can also be used but will not

detect increased blood glucose concentrations until they are above the renal threshold (14–16 mmol/L or 250–288 mg/dL). Similarly, although encouraged, careful monitoring of water intake and urine output to detect an increase does not provide early detection of persistent hyperglycemia below the renal threshold.

Glucose variability describes the degree of fluctuation in blood glucose concentration within a day, and also between days. It is best appreciated using continuous glucose monitoring systems. In diabetic cats, those with bigger differences between the maximum and minimum blood glucose (greater glucose variability) were more likely to have clinical signs, and hence a lower probability of remission.[22,23] Glucose variability is increased in cats with short duration of insulin action, concurrent diseases, in cats that do not achieve diabetic remission, if the insulin dose is changed frequently, and with day-to-day variability of dietary carbohydrate consumption (**Figure 1**). Glucose variability is reduced with low-carbohydrate diets and long-acting insulin, and often decreases over time prior to remission being achieved, because endogenous insulin secretion improves.[9]

MANAGING CATS IN DIABETIC REMISSION

Most cats in diabetic remission do not have normal glucose metabolism; 80% have impaired ability to normalize glucose concentrations after a glucose challenge (termed *impaired glucose tolerance*). Fewer (30%) have impaired fasting glucose, which are persistent glucose concentrations above normal but less than diabetic (> 117 to < 180 mg/dL; > 6.5 to < 10 mmol/L). Cats in remission with impaired fasting glucose or glucose intolerance have an 80% probability of relapsing within 12 months.[7] Maintaining a low-carbohydrate diet and continuing energy restriction to achieve an ideal body weight is critically important to reduce the probability of relapse.

Cats not previously diagnosed with diabetes but with impaired fasting glucose should be considered pre-diabetic and managed similarly to cats in diabetic remission. However, in most of these cats, blood glucose concentrations > 117 to < 180 mg/dL (> 6.5 to < 10 mmol/L) are dismissed as the result of stress. It is strongly recommended that in cats with other risk factors (> 8 years of age, overweight/obese, predisposed breed), additional testing is performed to differentiate pre-diabetes from stress hyperglycemia. This includes either measuring blood glucose concentrations after 4 hours using a minimally stressful method (e.g., from ear or pad sample), glycated hemoglobin, or interstitial glucose using a continuous glucose monitor in the home environment. Early diagnosis is important so these cats can be managed appropriately to prevent diabetes ensuing.

CONCLUSION

Clinicians should be prepared to offer flexible, practical, and individualized options for managing diabetes in cats. Regardless of the approach used, key factors include a low-carbohydrate diet, as well as consistent portion control to minimize day-to-day variation in dietary carbohydrate intake and to control calorie intake. In many newly diagnosed diabetic cats, the priority for management is to achieve diabetic remission because of the increased quality of life advantages for the client and cat. This is best achieved using a low-carbohydrate diet, long-acting insulin, and frequent monitoring and adjustment of insulin dose to achieve blood glucose concentrations that are normal or near normal, while avoiding clinical hypoglycemia.

In long-term diabetics, cats with other life-reducing comorbidities, and for owners who prefer a less intensive approach to monitoring, treatment is aimed at controlling clinical signs of diabetes, minimizing the risk of hypoglycemia, and managing any comorbidity. Dietary choice will be determined balancing the need to manage the comorbidity while avoiding signs of hyper- or hypoglycemia.

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HYPERLIPIDEMIA IN DOGS AND CATS

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KEY TAKEAWAYS

- Hyperlipidemia is more commonly secondary to other diseases such as endocrinopathies and obesity.
- Management of persistent hyperlipidemia requires appropriate dietary modifications (e.g., low-fat diets, high dietary fiber, niacin, omega-3 fatty acids).
- Some animals will not respond to dietary management alone and will require medical treatment.

DEFINITION

The term *hyperlipidemia* refers to an increased concentration of lipids (i.e., triglycerides, cholesterol, or both) in the blood. An increased blood concentration of triglycerides is referred to as *hypertriglyceridemia*, while an increased blood concentration of cholesterol is referred to as *hypercholesterolemia*.

CAUSES OF HYPERLIPIDEMIA

Secondary Hyperlipidemia

Postprandial hyperlipidemia is physiologic and typically resolves within 7 to 12 hours after a meal. Therefore, determination of serum lipid concentrations should always follow a fast of at least 12 hours.[1] Persistent fasting hyperlipidemia can be either primary or secondary to other diseases or drug administration. Secondary hyperlipidemia is the most common form of hyperlipidemia in dogs and cats. Most commonly, secondary hyperlipidemia is the result of an endocrine disorder, such as hypothyroidism, diabetes mellitus, or hyperadrenocorticism.[2-9] Hyperlipidemia has also been associated with naturally occurring pancreatitis in dogs.[2,3,10-12] Another important cause of secondary hyperlipidemia in dogs and cats is obesity.[13-16] Other possible causes of secondary hyperlipidemia in dogs and/or cats include protein-losing nephropathy, cholestasis, high-fat diets (dogs), hepatic lipidosis (cats), and possibly other conditions (e.g., infections, inflammation, neoplasia, congestive heart failure).[17,18] Administration of certain drugs (glucocorticoids, estrogens, phenobarbital, potassium bromide, and progestagens) can induce marked hyperlipidemia.[19]

Primary Hyperlipidemia

Primary lipid abnormalities in dogs are usually associated with certain breeds. Primary hyperlipidemia is very common in Miniature Schnauzers (>30% of Miniature Schnauzers are affected based on one study).[20-22] Primary hyperlipidemia has also been reported in Shetland Sheepdogs, Beagles, Briards, Doberman Pinschers, Rottweilers, and a family of rough-coated Collies from the United Kingdom.[23-28] Primary lipid abnormalities are uncommon in cats. Burmese cats have been reported to commonly have a familial form of lipoprotein metabolism disorder.[29,30]

CLINICAL CONSEQUENCES OF HYPERLIPIDEMIA IN DOGS AND CATS

Hyperlipidemia per se does not appear to lead to any clinical signs. However, many animals with hyperlipidemia develop diseases as a result of hyperlipidemia and clinical signs develop as a result of those diseases.

Pancreatitis

Hyperlipidemia, and more specifically hypertriglyceridemia, has long been suspected as a risk factor for canine pancreatitis,[10,11,17] and severe hypertriglyceridemia is a known risk factor for pancreatitis in Miniature Schnauzers.[31,32] No such evidence currently exists in cats.

Insulin Resistance

Evidence of insulin resistance has been documented in Miniature Schnauzers with primary hypertriglyceridemia.[33] In one study, almost 30% of Miniature

Schnauzers with primary hypertriglyceridemia had evidence of insulin resistance.[34] The association between hyperlipidemia, insulin resistance, and type 2 diabetes is not clear in cats.

Hepatobiliary Disease

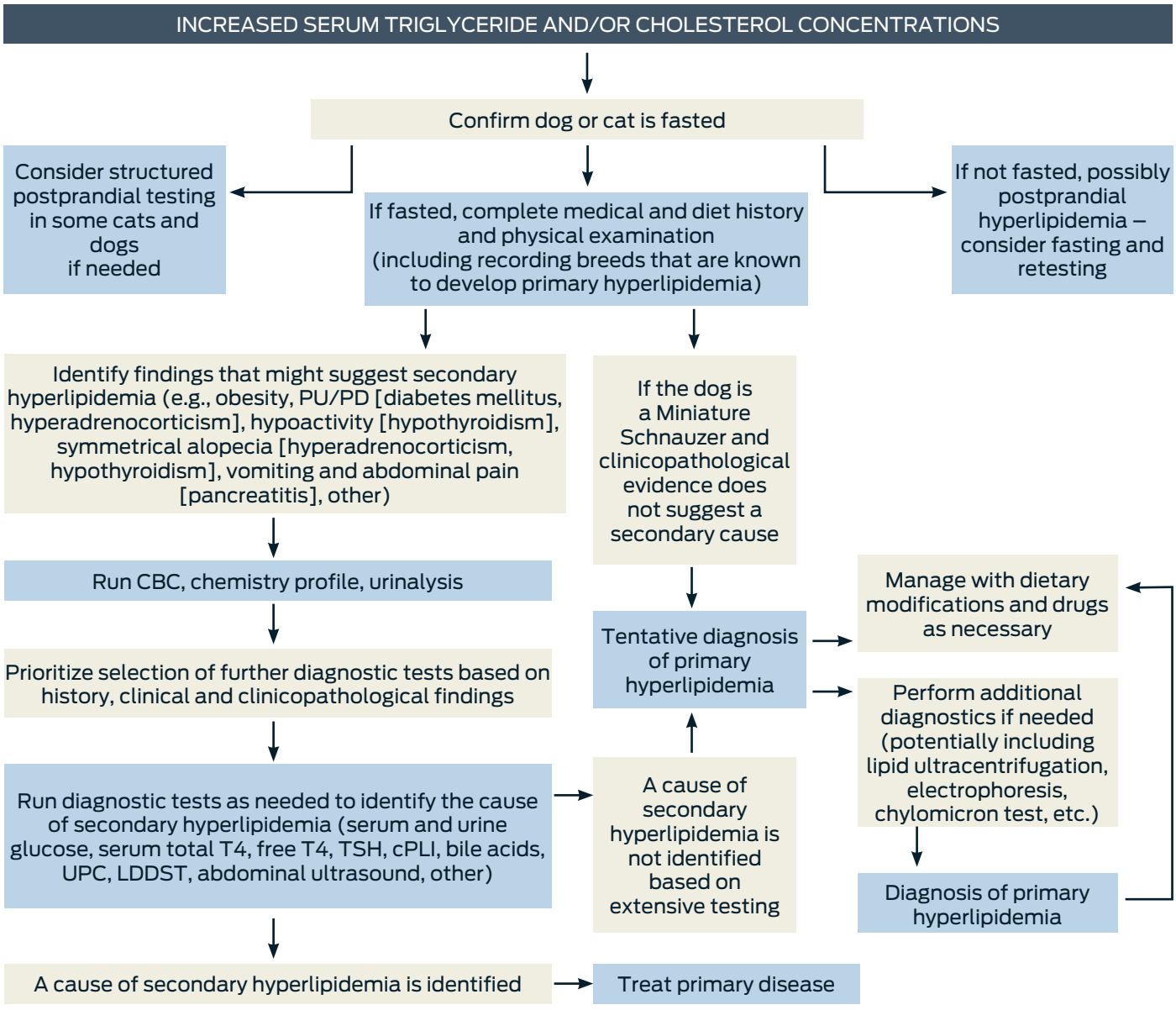
Clinical studies and anecdotal observations suggest that diffuse vacuolar hepatopathy and gallbladder mucocele are associated with hyperlipidemia in dogs.[17] In one study, 60% and 45% of the Miniature Schnauzers with serum triglyceride concentrations ≥ 4.52 mmol/L (400 mg/dL) had increased serum ALP and ALT activities, respectively.[35]

Other, less common, consequences of hyperlipidemia in dogs and cats may include atherosclerosis,[36-41] ocular disease (such as lipemia retinalis, lipemic aqueous, and lipid keratopathy),[29,30,42,43] xanthomatosis (benign granulomatous lesions), proteinuria and glomerular lipidosis,[44-46] neurologic disease (seizures, ischemic strokes, and other neurologic signs),[37,47-50] and a clinical syndrome of transient hyperlipidemia in kittens.[51-54]

DIAGNOSTIC APPROACH TO DOGS AND CATS WITH HYPERLIPIDEMIA

Hyperlipidemia is typically diagnosed by measurement of fasting serum triglyceride and/or cholesterol concentrations. The general diagnostic approach when evaluating dogs with hyperlipidemia is presented in **Figure 1**. After hyperlipidemia has been diagnosed, the next step is to determine whether the patient has a primary or a secondary lipid disorder. If hyperlipidemia

Figure 1. Management of hyperlipidemia in dogs and cats



is secondary, the condition causing hyperlipidemia should be diagnosed and treated. Thus, specific diagnostic investigations should be performed to diagnose or rule out specific diseases that can cause secondary hyperlipidemia (**Figure 1**). If causes of secondary hyperlipidemia are excluded, a tentative diagnosis of a primary lipid disorder can be made.

TREATMENT OF HYPERLIPIDEMIA

Treatment of secondary hyperlipidemia relies on the successful treatment of the underlying disorder. If hyperlipidemia does not resolve, another underlying cause, different or additional therapy, or concurrent primary hyperlipidemia should be considered.

In most cases, treatment should initially be pursued with dietary management, while drug therapy can be initiated later if deemed necessary. Nutritional strategies used for management of hyperlipidemia in dogs and cats are described in **Table 1**. Although the management of hypercholesterolemia seems to be of less clinical importance than that of hypertriglyceridemia in dogs and cats, severe hypercholesterolemia may be treated at least with dietary management.

Dietary Management

Low-fat diets: Typically, the first step in the management of primary or persistent secondary hyperlipidemia in dogs and cats is dietary modification. The most effective dietary option for hyperlipidemia in dogs is feeding a low-fat diet. Dogs with primary hyperlipidemia should be offered a low-fat diet throughout their lives. Unfortunately, the effectiveness of low-fat diets in the management of cats with hyperlipidemia is unknown. In addition, true low-fat diets are not commercially available for cats. The effect of long-term fat restriction on the general health of healthy and diseased cats is largely unknown.

Many commercially available diets are labeled as low-fat but their fat content can vary widely. It needs to be pointed out that the percentage of fat content of the diet (commonly listed on food labels) does not reliably reflect the amount of fat the animal is consuming. Therefore, fat content should be assessed on a metabolizable energy basis. The author generally recommends diets that contain less than 2.5 g of total fat per 100 kcal for dogs. In dogs with mild hyperlipidemia that are on high-fat diets, moderate fat restriction (e.g., 3.5 g of total fat per 100 kcal) might be adequate. In the only currently available study, Miniature Schnauzers with primary hyperlipidemia were fed a low-fat diet for 8 weeks.[55] By the end of the treatment period, there was a significant reduction in both serum triglyceride and cholesterol concentrations. Serum cholesterol concentrations returned to normal in all dogs, while serum triglyceride concentrations returned to normal

Table 1. Dietary modifications used for management of hyperlipidemia in dogs and cats

Dietary modification	Feeding amounts	Side effects	Comments
Low-fat diets	Fat < 2.5 g/100 kcal	None known	Cornerstone of treatment Effective in many cases Percent of fat in diet not accurate Dietary fat content should be evaluated on calorie content basis or percent metabolizable energy
Dietary fiber	Unknown	None known	Unknown effectiveness
Omega-3 fatty acids	200–300 mg/kg, q24 h, PO	Fishy odor, gastrointestinal signs	Questionable effectiveness
Niacin	50–100 mg/day (total dose)	Erythema, pruritus, myotoxicity, hepatotoxicity	Questionable effectiveness Possibly modest effect
Chitosan	3 g/cat q24 h, PO	None known	Limited experience Possibly modest effect
5-Aminolevulinic acid	1 mg/kg, q24 h, PO	None known	Exact effectivness unknown

in about 30% of dogs. However, all dogs that had serum triglyceride concentrations > 500 mg/dL (5.65 mmol/L) at the beginning of the study had serum triglyceride concentrations < 500 mg/dL (5.65 mmol/L) by the end of the trial. In cats, in the author's experience, canned high-protein, high-fiber, low-fat diets may be more efficacious than dry diets.

Homemade low-fat diets have not been systematically evaluated for the management of hyperlipidemia in dogs and cats. Some of these diets may have an even lower fat content (< 1.8 g per 100 kcal) than some commercially available low-fat diets. If such diets are used, care should be taken to make sure that these diets are complete and balanced, especially when intended for long-term feeding, and that the minimum nutrient requirements are met for all nutrients, including essential fatty acids. Treats and table scraps should be avoided unless they are low in fat and, if fed, should be kept at 10% or less of total daily calories.

COMMUNICATION TIP

"Typically, the first step in the management of primary or persistent secondary hyperlipidemia in dogs and cats is dietary modification."

In some dogs and cats, additional dietary modifications may be used if low-fat diets are not effective. These may include the following:

Dietary fiber: Complex carbohydrates seem to have a positive effect on lipid metabolism. Although explicit studies in dogs and cats are lacking, it might be possible, based on experience in humans and other animals, to achieve a reduction in blood lipid levels with the inclusion of dietary fiber in the diet. While insoluble fibers, such as cellulose, have a typical bulking effect, soluble fibers can, depending on their characteristics, lead to a change in the viscosity of the digesta and can also influence the composition and metabolic activity of the intestinal microbiota. However, there is ample need for research in this area to determine the optimal dosage at which fiber should be included in a diet for dogs and cats with hyperlipidemia.

Omega-3 fatty acids: Omega-3 fatty acid (eicosapentaenoic acid [EPA] and docosahexaenoic acid [DHA]) supplementation has been shown to lower serum triglyceride concentrations in experimental animals and humans, including cases of primary hypertriglyceridemia.[56] The mechanisms of the lipid-lowering action of omega-3 fatty acids are complex and include regulation of several transcription factors that lead to reduced lipogenesis, increased β-oxidation, and activation of lipoprotein lipase.[56,57] In a study of healthy dogs, fish oil supplementation led to a significant reduction of serum triglyceride concentrations.[58] Studies evaluating the efficacy and safety of omega-3 fatty acid supplementation in dogs or cats with hyperlipidemia are lacking. A "fishy" odor is often noted in dogs receiving high doses of omega-3 fatty acids and it might be unacceptable for some owners. EPA and DHA may be used in dogs and cats at doses ranging from 200 to 300 mg/kg, PO, once a day, and their effect on serum triglyceride concentrations is dose dependent. Their lipid-lowering effect typically requires doses at the high end of the recommended dose for dogs. An upper daily limit of 4 to 5 grams of total omega-3 fatty acids might be recommended, and the NRC safe upper limit of 280 mg of EPA+DHA per 100 kcal fed should not be exceeded for dogs.[59] There is no established safe upper limit for cats.

Niacin (nicotinic acid): Niacin is a form of vitamin B3 that has been used successfully for the treatment of hyperlipidemia in humans for many years.[60] When used in pharmacological doses, niacin is a broad-spectrum lipid-modifying drug.[57] The mechanism of action of niacin is complex and incompletely understood but includes inhibition of hormone-sensitive lipase activity and the enzyme diacylglycerol acyltransferase.[57] Clinical trials on the efficacy and safety of niacin in dogs and cats with primary hypertriglyceridemia are lacking and clinical experience is limited. In some dogs, niacin reduced serum triglyceride concentrations for several months without causing any side effects.[61] As is often the case in humans, niacin administration in dogs and cats may be associated with side effects such as erythema and pruritus, which may require discontinuation of therapy. Long-term risk for myotoxicity and hepatotoxicity may also exist.[57] Niacin may be administered to dogs and cats at a total dose of 50 to 100 mg/day. Both the therapeutic and side effects of niacin are dose dependent, and it is therefore recommended that niacin is started at a low dose and slowly titrated upward (every 4 weeks) based on the

results of follow-up serum cholesterol and triglyceride concentrations.

Chitosan: Chitosan is a natural compound derived from the polysaccharide chitin and appears to bind to negatively charged lipids in animal trials, hence reducing their gastrointestinal uptake and lowering serum cholesterol. One study has evaluated the use of chitosan (3 g/cat once a day) in a small number of cats with induced hyperlipidemia.[62] Chitosan was found to be effective in reducing both serum triglyceride and cholesterol concentrations, although concentrations did not seem to normalize in some of the cats.

5-Aminolevulinic acid: 5-Aminolevulinic acid (5-ALA) is a natural δ-amino acid that has been hypothesized to improve lipid and glucose metabolism in obese mice. In a recent study, 5-ALA was used in five Miniature Schnauzer dogs with severe hypertriglyceridemia and was found to significantly lower (but not normalize) serum triglyceride concentrations.[63]

Not all dietary options should necessarily be tried before medical management is initiated. Serum lipid concentrations should be re-evaluated every 3 to 4 weeks after any dietary modification. If additional reduction of serum triglyceride concentration is desired, additional dietary modifications or medical treatment should be considered.

Medical Management

Some animals with hyperlipidemia may not sufficiently respond to dietary modification or faster, and more predictive lowering of serum lipid concentrations may be required. In these cases, medical treatment may be required.

Fibrates (fibric acid derivatives): Fibrates suppress fatty acid synthesis, stimulate fatty acid oxidation, activate lipoprotein lipase, and inhibit noncompetitively the enzyme diacylglycerol acyl transferase 2 (the enzyme that catalyzes the conversion of diglycerides to triglycerides), therefore leading to an overall reduction in serum triglyceride concentration.[56,57,64] Gemfibrozil has been anecdotally used in the past but, in the author's experience, many canine patients with primary hyperlipidemia do not respond well. Bezafibrate has been evaluated for the treatment of hyperlipidemia of various causes (both primary and secondary) in dogs and was found to be highly effective in reducing serum triglyceride and cholesterol concentrations.[65,66] Fenofibrate was also evaluated in the treatment of severe hypertriglyceridemia in dogs (both primary and secondary) and was found to be highly effective.[67] No studies have evaluated the safety and efficacy of fibrates in cats. Periodic testing of serum triglyceride concentration and liver enzyme activities is recommended.

Statins: Statins are mainly cholesterol-lowering drugs (in humans they specifically lower LDL-cholesterol) with less potent effects on triglyceride metabolism.[57,64] In a recent study, the pharmacokinetics of simvastatin were described in healthy Beagle dogs.[68] However, this drug has not been tested in dogs with hyperlipidemia. In a small study in cats (n=7) in which hyperlipidemia was induced through feeding of cholesterol powder, atorvastatin was effective in significantly reducing (and possibly normalizing) both serum triglyceride and cholesterol concentrations compared with controls.[62] In animals in which statins are used, serum hepatic enzyme activities should be periodically monitored for potential hepatotoxicity.

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GASTROINTESTINAL DISORDERS

ASSESSING AND MANAGING THE GUT MICROBIOME IN CANINE AND FELINE PRACTICE

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KEY TAKEAWAYS

- Dysbiosis is often an early biomarker of an abnormal gut environment
- Significant dysbiosis, often with reduction of *C. hiranonis*, frequently occurs secondary to chronic enteropathy or after broad-spectrum antibiotic use
- Dysbiosis is often a component of chronic intestinal changes on the mucosal level, and a multi-modal therapy approach addressing the underlying GI disease along with the dysbiosis should be attempted

DEFINITIONS

Intestinal Microbiome

The intestinal microbiome is the collective of all microorganisms within the gastrointestinal tract (GIT). Bacteria make up the majority with >95% of microorganisms. It is an important immune and metabolic organ, as bacteria convert dietary compounds (e.g., fiber, protein, fat) or host molecules (e.g., bile acids) into metabolites that affect function of the intestine and also other organ systems.

Major microbiota-derived metabolites include short chain fatty acids (SCFA), indoles, and secondary bile acids (BA). SCFA are substrates that can be catabolized and therefore serve as an energy source, and can also be used by other bacteria in the gut. SCFA are also anti-inflammatory and modulate intestinal motility and improve gut barrier function. Some bacteria (e.g., *Faecalibacterium*) ferment dietary carbohydrates to SCFAs.

Intestinal bile acid conversion is particularly important in maintaining a normal microbiome.[1,2] Briefly, primary BAs from the liver that escape ileal uptake and enterohepatic circulation and reach the colon are converted to secondary BAs by *Clostridium hiranonis*.[3,4] Secondary BAs in physiological amounts act as signaling molecules, have glucose-lowering effects, and are anti-inflammatory.[5] They suppress potential enteropathogens such as *C. difficile*, *C. perfringens*, and *E. coli*.[6] A lower abundance of *C. hiranonis* and decreased conversion of primary to secondary BAs is strongly associated with intestinal dysbiosis in dogs and cats.[1,4,7]

Dysbiosis

The intestinal microbiota is in contact with the intestinal epithelium, mucus layer, and immune system. Changes in these will affect microbiota composition, and dysbiosis is often an early biomarker of an abnormal gut environment at the mucosal level in chronic inflammatory enteropathies (CE). Intestinal dysbiosis encompasses either a reduction in microbial diversity (i.e., reduction in the number of different species) and/or changes in bacterial abundances that lead to altered production of bacteria-derived metabolites.[8,9] Dysbiosis patterns differ based on the underlying causes (see **Figure 1**). Significant dysbiosis, often with reduction of *C. hiranonis*, occurs often secondary to CE[3] or after broad-spectrum antibiotic use[1,10] and can contribute to clinical signs in some patients, but can also be subclinical. Dysbiosis is assessed together with the overall clinical history, physical examination, and other diagnostic testing to arrive at a holistic assessment of the GIT.

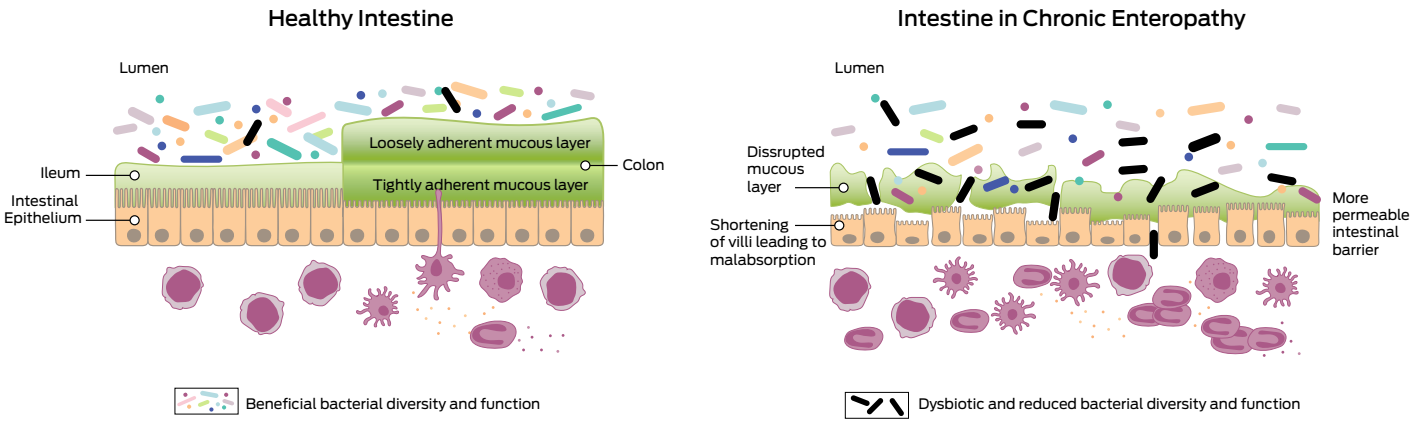
MICROBIOME ASSESSMENT

Dysbiosis Index (DI)

The DI is a commercially available, analytically validated, PCR-based assay to assess the canine and feline microbiome in individual patients (https://tx.ag/DysbiosisGI).[2,11] The DI quantifies the fecal abundance of specific bacterial taxa, provides reference intervals for these, and additionally calculates a single number

Figure 1. The intestine in health and disease. A healthy intestine (left) is characterized by a balanced microbiome, an established mucus layer (green) separating luminal bacteria from the epithelial cells, a normal epithelial cell barrier, and a regulated immune system.

In chronic inflammatory enteropathy (right), various changes may occur, with all of them potentially contributing to clinical signs. Loss of mucus allows luminal bacteria to attach to epithelial cells, stimulating pro-inflammatory cytokines. A broken barrier leads to translocation of food and bacterial antigen, which also activates the immune system. Loss of transporters in the brush border leads to malabsorption of dietary compounds, which can lead to bacterial overgrowth. The inflammation (changes in pH and oxygen on mucosal surface) and the low-grade malabsorption of nutrients (provides substrate for bacterial overgrowth) both can contribute to intestinal dysbiosis.



that expresses the extent of shifts in the microbiome (**Figure 2**). The DI correlates negatively with species richness (i.e., a higher DI indicates lower microbial diversity).[1]

The DI is interpreted together with the abundance of the individual bacteria, especially that of *Clostridium hiranonis*, as a decrease in the abundance of this species is a major contributor to an abnormal intestinal microbiome.[6,7] A DI above 2 (dogs) or 1 (cats) indicates a significant dysbiosis, while a DI between 0 and 2 (dogs) and 0 and 1 (cats) indicates a mild to moderate microbiome shift. Some animals have a DI<0, but with some bacteria outside their respective reference intervals, and this suggests minor changes. A very high DI is often seen in in refractory GI disease and may reflect the severity of intestinal changes on the mucosal level.

The DI is also useful for screening donors for fecal microbiota transplantation (FMT), as a subset of clinically healthy animals may have subclinical dysbiosis, potentially due to underlying intestinal changes. Also, animals with non-specific clinical signs (i.e., lack of diarrhea and/or vomiting) may have an increased DI which may aid to identify the presence of chronic enteropathy, especially in cats.[2]

Animals should be off treatment with omeprazole and/or antibiotics prior to measurement of the DI (**Figure 2**). Omeprazole leads to a transient increase in the DI, but with normal counts of *C. hiranonis*. The DI normalizes within 1–2 weeks after discontinuation of omeprazole therapy. Broad-spectrum antibiotics (i.e., tylosin and metronidazole) induce severe dysbiosis. The microbiota typically normalizes within 2–4 weeks after discontinuation of antibiotics in most animals, but some may have persistent dysbiosis. Also, some animals on homemade high protein / high fat raw meat-based diets but low fiber content may have a mildly increased DI, but with normal counts of *C. hiranonis*.[12]

Bacterial Culture

Fecal culture is not useful to assess the microbiome, as it is not standardized and because the majority of bacteria are strict anaerobes that require specialized growth media. A recent study showed no agreement in reported culture results between reference laboratories.[13] However, culture can be used for testing of specific cultivable pathogens, (i.e., *Salmonella* or adherent-invasive *E. coli* in confirmed cases of granulomatous colitis) combined with antimicrobial susceptibility profiling.

COMMUNICATION TIP

While pets with diarrhea may show initial clinical improvement with antibiotics, bacteria will often regrow after therapy, causing relapse.

Sequencing of 16S rRNA Genes

Sequencing is offered commercially to assess the microbiome in individual patients. Furthermore, based on the results, "tailored" microbiome-modulating therapies are recommended. No studies have been published that report how reference intervals have been established, and how these compare between healthy and diseased animals. Sequencing-based techniques lack reproducibility and are therefore generally not suited for assessment of individual patients over time. Furthermore, there is no data currently available that is able to predict, based on microbiome assessment alone, which microbiome-modifying therapy would be useful in individual patients with chronic enteropathies.

THERAPEUTIC APPROACHES TO DYSBIOSIS

General Considerations

It is important to note that due to the large number of bacteria present in the GIT, estimated at around 100 trillion bacterial cells, it is very difficult to directly induce major shifts in the microbiota. Consequently, because dysbiosis is often a component of chronic intestinal changes on the mucosal level, a multi-modal therapy approach addressing the underlying GI disease along with the dysbiosis should be attempted.[14] Therapy should consist of dietary manipulation as the first-line treatment, which can then be combined as needed with additional strategies such as probiotics, prebiotics, fecal microbiota transplantation (FMT), and in rare cases antibiotics.[15,16] An increased DI and reduced counts of *C. hiranonis* in animals with CE often remains abnormal for several months to years, even if animals are in clinical remission. This is likely due the fact that the dysbiosis remains because of the persistent changes on the mucosal level (**Figure 1**) and indicates persistent dysfunction of the intestine.[6,17,18] Nutritional therapy may modify the substrate available for intestinal bacteria which leads to improvement in clinical signs, but it does not directly reduce the dysbiosis. Also, anti-inflammatory therapy with corticosteroids in dogs with CE, aimed at treating the underlying intestinal inflammation, was shown to reduce the DI and normalize *C. hiranonis* over several months.[17]

Only FMT leads to quick normalization of the microbiome (i.e., decreases the DI in a few days) in many cases, but the long-term resolution of the dysbiosis may depend on the underlying disease process (see below).[19]

Dietary Manipulation

Various diet types (e.g., highly digestible gastrointestinal, hydrolyzed protein diets, fiber-enriched, and novel protein diets) have been shown to induce clinical remission in animals with CE. While the exact mechanism is unknown, a highly digestible diet reduces undigested nutrients in the GI lumen, reducing the potential for excessive bacterial proliferation. Commonly used hydrolyzed protein or novel protein diets have typically high digestibility, although the primary goal with hydrolyzed protein diets is to identify and manage dogs and cats with food-responsive enteropathies. Although fiber-enriched gastrointestinal diets are not highly digestible overall, the raw materials providing macronutrients such as protein are typically also highly digestible, and together with the fiber component this can modulate the intestinal microbiota. Some studies have associated clinical remission in food-responsive enteropathies with partial, but not complete, normalization of the microbiome over several months.[6,18,20]

Prebiotics

Prebiotics are indigestible carbohydrates that promote growth of beneficial microorganisms, and can be divided into soluble/non-soluble and fermentable/non-fermentable fibers.[21] Fermentable prebiotics are converted by colonic bacteria to SCFA, which have multiple beneficial effects as described above. Most commercial GI diets contain prebiotics, but for some patients, additional fiber supplementation (e.g., psyllium husk) can be beneficial.

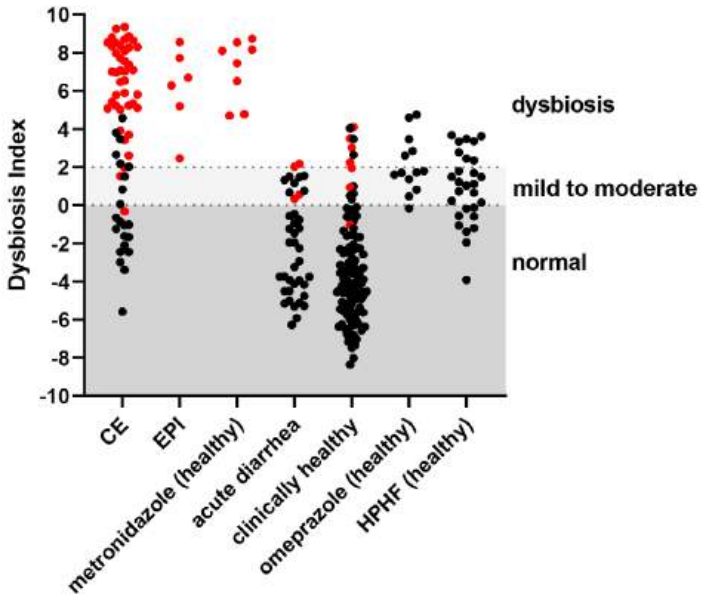


Figure 2. Dysbiosis Index (DI) in dogs. Dogs in red have reduced abundance of *C. hiranonis*, a beneficial bacterium important for maintaining a normal microbiome. The DI is interpreted together with the individual bacterial taxa. A DI>2 represents a major shift (i.e., dysbiosis), a DI between 0 and 2 indicates a moderate shift. Some dogs have a DI<0, but with some bacteria outside the reference intervals, suggesting minor changes.

The patterns differ between dogs with chronic enteropathy (CE)[8] and exocrine pancreatic insufficiency (EPI),[31] as these dogs have often increased DI with a reduced *C. hiranonis.* A small subset of dogs with acute diarrhea have a mild shift in the microbiome which typically normalizes within a few days.[32] Dogs on metronidazole[1] and tylosin[10] show severe dysbiosis. A small subset of healthy dogs has subclinical dysbiosis, while healthy dogs on omeprazole[33] and on a homemade high protein / high fat (HPHF) raw meat-based diet[12] can have an increased DI but normal counts of *C. hiranonis.*

Probiotics

Probiotics are live bacteria, which when administered in adequate amounts confer a health benefit on the host. Empirical administration of probiotics should be considered as an ancillary treatment in dogs with CE. It is important to note that the effects of probiotics are strain-specific, and it is currently recommended that only probiotic products from reputable manufacturers and products that have a demonstrated benefit in clinical studies in dogs or cats should be used.

There are only a few commercially available formulations that have been evaluated in clinical studies. For example, *Enterococcus faecium* SF68 significantly lowered the percentage of shelter cats having diarrhea lasting longer than two days.[22] *E. faecium* SF68 combined with metronidazole also significantly reduced duration of acute diarrhea in shelter dogs when compared with metronidazole alone (two vs. four days)[23] and reduced the severity of diarrhea in healthy cats receiving amoxicillin/clavulanic acid.[24] A multiple probiotic strain mixture combined with a prebiotic improved fecal scores in cats with chronic diarrhea.[25] A high potency multi-strain probiotic used as an adjunct to prednisone therapy was shown to be associated with an increased expression of tight junction protein, suggesting improvement in intestinal barrier function in dogs with CE.[26] The same formulation also led to more rapid normalization of the intestinal microbiota in dogs with acute hemorrhagic diarrhea.[27]

Antibiotics

Tylosin or metronidazole are often used in dogs or cats with chronic GI diseases. They can lead to improvement of clinical signs, but patients frequently relapse after the end of treatment.[28] The likely explanation for this is that while antibiotics lead to a reduction of bacterial load and clinical improvement,[29] bacteria will often regrow after therapy. Antibiotics also cause intestinal dysbiosis that can last for months.[1,4,10] Therefore, it has been proposed that antibiotics should only be considered in animals after they have failed dietary and anti-inflammatory trials or in patients with signs of systemic inflammation.[15]

Fecal Microbiota Transplantation (FMT)

FMT is the transfer of stool from a healthy donor into the gut of a recipient via oral capsules, endoscopy, or enema. FMT is an emerging therapy, and the success appears to depend on the underlying disease process. In dogs with CE, dysbiosis is often secondary to the intestinal inflammation and structural damage. Recurrence of dysbiosis and clinical signs will occur when the underlying pathology is still present. Therefore, FMT has a variable success rate in dogs and cats with CE. Anecdotal reports suggest many dogs

with CE will have improvement in fecal scores within two to three days; clinical signs will often relapse, but the time to relapse can vary significantly between individual animals. Therefore, repeated FMTs can be useful as adjunct treatment in animals with refractory chronic enteropathy not responding satisfactory to standard therapy. Initial data would suggest that the more extensive the dysbiosis (the higher the DI), most likely reflecting the severity of intestinal changes, the more rapidly relapses will occur. Therefore, in these patients, dietary and anti-inflammatory treatment of the underlying disease process is required (see above), and FMT can be considered as adjunct treatment for patients with suboptimal response to standard therapy.[4,30] In animals with antibiotic-induced dysbiosis or acute diarrhea and no evidence of underlying intestinal disease, the DI remains typically normal for extended periods and is associated with normalization of clinical signs.[4]

CONCLUSION

The intestinal microbiome plays a crucial role in host health. Many animals with GI disease have dysbiosis that results in abnormal microbial function. As intestinal dysbiosis can have different underlying causes, multimodal therapeutic approaches are necessary to normalize intestinal microbiota composition.

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PRACTICAL TOOL: PREBIOTICS, PROBIOTICS, SYNBIOTICS, AND POSTBIOTICS

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The gut microbiome can be influenced by many factors including, but not limited to, diet, dietary supplements, and the presence of gastrointestinal or other diseases. The effects of the gut microbiome on canine and feline health are widespread but are not fully understood. The gut microbiome is a widely discussed topic, and microbiomes exist in other systems, such as the skin and oral cavity. The purpose of this tool is to review definitions of prebiotics, probiotics, synbiotics, and postbiotics, which are intended to positively influence the microbiome (**Table 1**). The focus of these definitions is on gastrointestinal health, but please note that other systems may benefit as well. All products utilized in practice should be supported by evidence to provide a health benefit for the patient, assessed for quality and safety, and studied for the intended use in a specific species.

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Table 1. Prebiotics, probiotics, synbiotics, and postbiotics

	Prebiotic	Probiotic	Synbiotic	Postbiotic
ISAPP Definition[1]	A substrate that is selectively utilized by host microorganisms conferring a health benefit on the host	Live microorganisms that, when administered in adequate amounts, confer a health benefit on the host	A mixture, comprising live microorganisms and substrate(s) selectively utilized by host microorganisms, that confers a health benefit on the host	A preparation of inanimate microorganisms and/or their components that confers a health benefit on the host
Contains Viable Microorganisms?	No	Yes	Yes	No
Suggested Functions and Benefits	Improve digestive function, support the immune system, selective enhancement of specific beneficial microorganisms, increase short-chain fatty acid production	Support immune function, aid digestion, help keep balance between beneficial and potentially pathogenic bacteria, produce certain vitamins Benefits are highly dependent upon the strain of probiotic Examples of benefits include reduction in severity of diarrhea, decreasing the negative effect of antimicrobials on the gut, and reducing some anxious behaviors Some probiotics support the gut microbiome when it is challenged, such as by antibiotics, stress, or dietary indiscretion	Depending on the synbiotic, the microorganism and the substrate may be complementary or synergistic The exact benefits depend on the combination provided Complementary: each component works independently to provide health benefit(s) Synergistic: the components work together to provide health benefit(s)	Postbiotic products for dogs and cats are an emerging area of research Examples of potential benefits seen in humans include decreased gastrointestinal signs such as diarrhea, reduced signs of anxiety, and improved clearance of infection[2] Initial research has suggested postbiotics support gastrointestinal and immune system health in dogs[3]
Other Information	Most prebiotics are dietary fibers Prebiotics may be added to pet foods or supplemented to provide benefits Examples include inulin, chicory root, and psyllium	Present in many supplements and some pet foods Probiotics should be chosen based on the desired effect and the evidence of the probiotic's efficacy in the target species Not all strains are equal; different strains have different effects Examples include *Enterococcus faecium* SF68, *Bifidobacterium longum* BL999, and *Bacillus coagulans* BC30	Most synbiotics currently available contain a prebiotic combined with a probiotic	Postbiotics are derived from microorganisms, but are free of viable organisms Postbiotics are not dead probiotics Postbiotics can be derived from probiotics, but this is not always the case If the postbiotic is derived from a probiotic, the postbiotic may have different effects versus the probiotic

PRACTICAL TOOL: PURINA FECAL SCORING CHART

Fecal consistency is primarily a function of moisture in stool and can be used to identify changes in colon health and other problems. In a healthy dog or cat, stools ideally should be firm but not hard, pliable, segmented and easy to pick up (Score 2).

Score	Specimen	Characteristics
1		■ Very hard and dry ■ Often expelled as individual pellets ■ Requires much effort to expel from the body ■ Leaves no surface residue when picked up
2		■ Firm, but not hard; pliable ■ Segmented appearance ■ Leaves little or no surface residue when picked up
3		■ Log shaped; moist surface ■ Little or no visible segmentation ■ Leaves surface residue, but holds form when picked up
4		■ Very moist and soggy ■ Log shaped ■ Leaves surface residue and loses form when picked up
5		■ Very moist, but has a distinct shape ■ Present in piles rather than logs ■ Leaves surface residue and loses form when picked up
6		■ Has texture, but no defined shape ■ Present as piles or spots ■ Leaves surface residue when picked up
7		■ Watery ■ No texture ■ Presesnt in flat puddles

PURINA Institute
Advancing Science for Pet Health

RT/CRCT

SMALL AND LARGE BOWEL DIARRHEA IN DOGS AND CATS

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KEY TAKEAWAYS

- Localization of the likely cause of diarrhea, small, large, or mixed-bowel, will enable a better diagnostic and therapeutic approach.
- Antibiotics are not recommended for the treatment of acute, uncomplicated diarrhea. Highly digestible diets including those containing fiber supplementation are a safer alternative for the patient.
- Acquisition of a dietary history is a critical component of the dietetic approach to chronic, idiopathic diarrhea in dogs and cats.

DEFINITION AND CHARACTERIZATION

Diarrhea is defined as an alteration in stool consistency, frequency, volume, and/or weight. More subtle signs of diarrhea, especially in animals with unsupervised access to the outdoors, may go unnoticed until a severe alteration in stool consistency or frequency develops. Characterizing the duration of diarrhea requires a detailed inquiry of the pet's history including a report on historical and current stool quality using a fecal scoring system (Practical Tool: Fecal Scoring Charts for Dogs and Cats). Based on this inquiry, the duration of diarrhea can be classified as acute, acute on chronic, or chronic. *Acute diarrhea* is generally defined as one or more episodes of diarrhea lasting less than 3 weeks. *Chronic diarrhea* is defined by the presence of persistent or intermittent diarrhea for longer than 3 weeks. *Acute on chronic diarrhea* is defined by the presence of acute diarrheic episodes in an animal with ongoing gastrointestinal disease. The diagnostic and therapeutic approach to diarrhea should be based on the duration of diarrhea as well as the signalment of the animal, diet and animal-specific history including concurrent gastrointestinal (GI) and systemic clinical signs, physical examination findings, and the likely origin of the diarrhea (i.e. small, large, mixed bowel). **Table 1** outlines the classification of the diarrhea according to its suspected origin. In the author's experience, the color of the bowel movement, apart from the presence of blood or lack of color (acholic feces), is rarely helpful and is heavily influenced by the animal's diet and medications.

Often, animals presented for evaluation of diarrhea have concurrent clinical signs including bloating and early satiety, change in appetite or food-seeking behavior ("dysorexia"), regurgitation, halitosis, vomiting, abdominal pain, coprophagia, or pica. All clinical signs and their relationship to time of day and activities, including feeding and exercise, are

Table 1. Characteristics of diarrhea and accompanying clinicals signs according to origin of disease

Origin	Weight loss	Dysorexia/ Nausea	Pain	Urgency/ Frequency	Volume	Mucus	Blood
Small	+/-	+/-	+/-	Normal	Normal to increased	+/-	+/- melena*
Large	-	-	+/-	Increased	Decreased	+ to +++	+/- hematochezia
Mixed	+/-	+/-	+/-	Normal to increased	Normal to decreased	-/+	+/- either melena or hematochezia

*Animals with distal small intestinal bleeding or rapid intestinal transit may occasionally have hematochezia rather than melena.

important to note as they will impact the nutritional and pharmacologic approach.

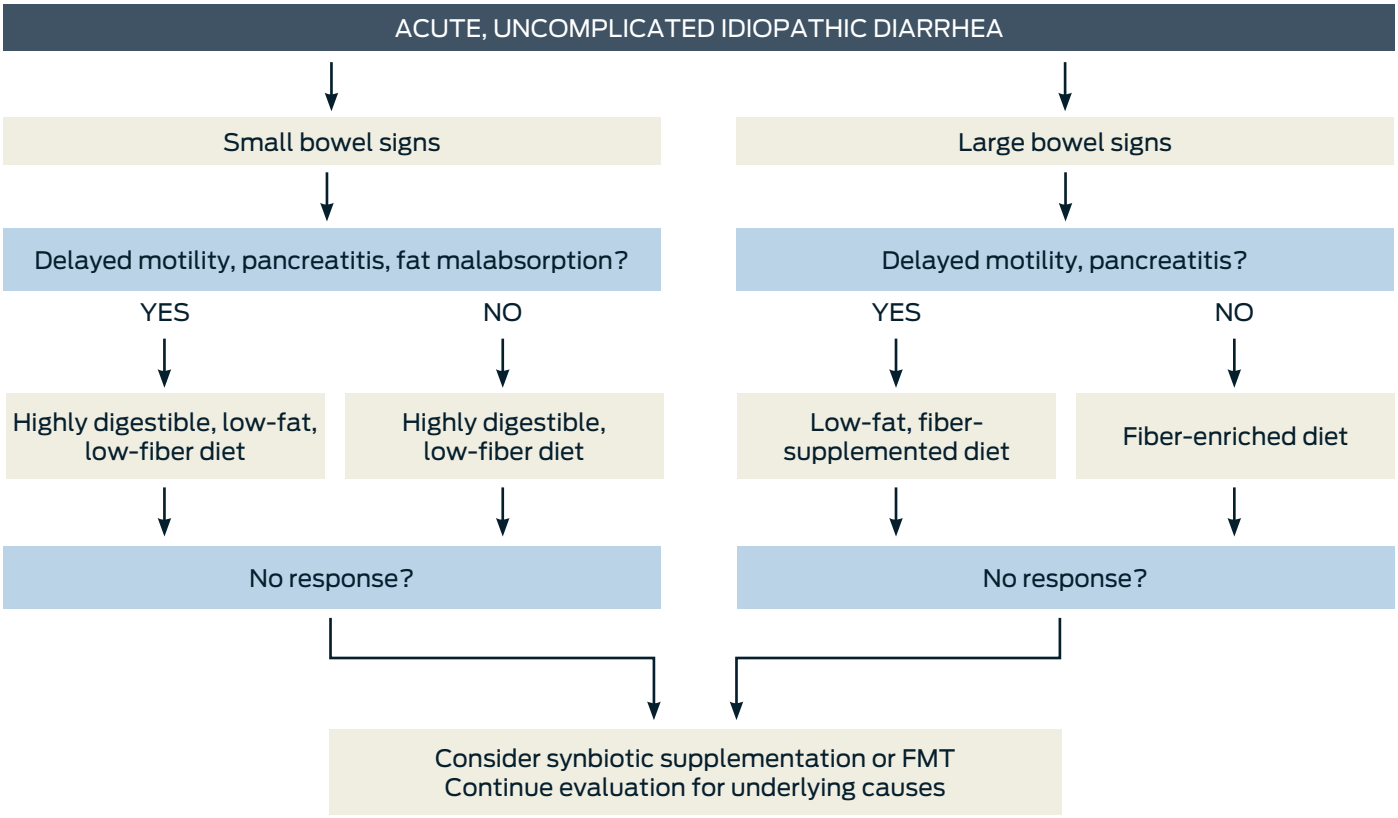
Acute Diarrhea

Evaluation for underlying systemic and gastrointestinal causes of acute diarrhea such as acute pancreatitis, gastrointestinal parasitism, or viral infection should occur alongside the therapeutic approach. Depending on the signalment, history, and physical examination findings, diagnostic tests that may be considered include fecal flotation and/or fecal PCR for helminths, fecal wet mount, Giardia ELISA, Parvo SNAP and/or PCR (dogs only), complete blood count, serum biochemistry, testing for hypoadrenocorticism (dogs only; e.g., urine cortisol:creatinine ratio, baseline cortisol, ACTH stimulation test), and abdominal imaging. A more detailed diagnostic approach to acute diarrhea can be found in other reviews.[1] Animals with mild forms of acute uncomplicated idiopathic diarrhea, especially those with a history of dietary indiscretion, and with no abnormalities on physical examination or fecal testing often need very little intervention other than time. However, owners rarely accept the "wait it out approach." Therefore, feeding a highly digestible, low-fiber diet such as a therapeutic gastrointestinal veterinary diet, in the case of small bowel diarrhea, or a highly digestible, fiber-enriched diet, in the case of large bowel (**Figure 1**), for a few days is a benign intervention that can improve rapidity of recovery.[2,3] Probiotics or synbiotics, oral intestinal adsorbents (e.g., smectite clay, kaolin-pectin), or loperamide are generally considered to be less effective than dietary intervention but may also be considered in select cases, especially in conjunction with a highly digestible gastrointestinal diet, and are described below (see nutrition versus medical intervention). Animals with severe, unrelenting diarrhea often need more intensive intervention and hospitalization with rehydration and restoration of electrolyte imbalances (see key nutrients). In malnourished animals or those with prolonged (> 3 days) anorexia necessitating hospitalization, early enteral nutrition (nutrition provided within 48 hours of admission) should be a central focus once the patient is hemodynamically and, ideally, metabolically stable.

Chronic Diarrhea

The most effective treatment for chronic diarrhea comes with identification of the underlying cause.

Figure 1. Dietary approach to acute, uncomplicated, idiopathic diarrhea. FMT, fecal microbial transplantation



However, often the cause cannot be determined in spite of exhaustive exploration, and a stepwise approach to nutritional intervention is necessary. Like acute diarrhea, the diagnostic approach to chronic diarrhea depends on the signalment, history (including dietary history), and physical examination findings. Diagnostic tests to evaluate for causes of chronic diarrhea may include fecal testing (e.g., fecal flotation, fecal helminth PCR, fecal cytology, Baermann, sedimentation, *Tritrichomonas foetus* PCR [cats only] and other geographic-specific infectious testing), FeLV/FIV (cats only), complete blood count, blood chemistry, urinalysis, abdominal imaging, pancreatic lipase immunoreactivity, trypsin-like immunoreactivity, testing for hypoadrenocorticism (dogs only; e.g., urine cortisol:creatinine ratio, baseline cortisol, ACTH stimulation test), and acquisition and evaluation of intestinal biopsies. A full review on the diagnostic approach to chronic diarrhea can be found elsewhere.[4] When the etiology of enteropathy has not yet been determined and the signs persist despite anthelmintic therapy, dietary modification (low-fat, highly digestible, fiber-enriched, novel protein, limited ingredient, hydrolyzed, or amino acid-based) is recommended. The decision of what type of diet to recommend is based on the signalment, previous dietary history and associated response, severity and presumed location of disease, and consideration of the nutritional factors that may be impactful to the individual patient as described in **Tables 2** and **3** and below. Like with other chronic disease states such as diabetes mellitus, clients should be educated that most animals with chronic idiopathic diarrhea will have occasional flares. Strategies such as those listed below to help controls these flares prior to their escalation should be discussed.

KEY NUTRIENTS AND NUTRITIONAL FACTORS FOR MANAGEMENT OF DIARRHEA

Hydration and Restoration of Electrolyte Imbalances

Dehydration and electrolyte shifts including hypokalemia, hypochloridemia, hyponatremia, and/or hypomagnesemia are often observed especially in dogs and cats presenting with severe diarrhea and inappetence.[5] Dehydration, hypovolemia, and, when possible, electrolyte derangements should be corrected prior to nutritional intervention. Rehydration will also allow for better assessment of the severity of an animal's anemia and blood protein deficit, if present. Most veterinary therapeutic gastrointestinal diets are enriched with electrolytes and meet or exceed the AAFCO- and FEDIAF-recommended levels for potassium, magnesium, sodium, and chloride for healthy animals. Typical nutrient analyses obtained from product information guides can be helpful to determine which diet is best based on the patient's assumed or recognized deficits. Glucose-based oral rehydration solutions contain a large amount of sugar

Table 2. Nutritional factors of concern for small bowel diarrhea

Key Nutritional Factors	Rationale
Protein	Protein source: novel, limited ingredient, hydrolyzed, or amino acid-based for possible food-responsive enteropathy. Hydrolyzed proteins contain fragments of protein allergen which are too small to stimulate immune response.
Fat	If ileus, pancreatitis, delayed gastric emptying, lymphangiectasia, or hyperlipidemia present, lower dietary fat (<3 grams fat*/100 kcal ME). Consider EPA/DHA supplementation to help reduce inflammation once clinical signs are controlled.
High total digestibility	A highly digestible diet will allow for increased digestion and absorption of nutrients in the small bowel.
Feeding frequency	Consider multiple (3-4) meals throughout the day to help with volume intolerances.

*When known, magnitude of reduction of dietary fat should be based on the previous quantity of dietary fat fed.

Table 3. Nutritional factors of concern for chronic large bowel diarrhea

Key Nutritional Factors	Rationale
Protein	Protein source: novel, limited ingredient, hydrolyzed, or amino acid-based due to possible food-responsive enteropathy. Hydrolyzed proteins contain fragments of protein allergen which are too small to stimulate immune response.
Mixed fiber sources	Bulking (insoluble) and absorbing (soluble, viscous) to help mitigate diarrhea. Fermentable fibers promote short-chain fatty acid production, which can improve colonocyte blood flow, health, and water absorption.
High total digestibility	In a compromised colon, a highly digestible diet will allow for increased digestion and absorption of nutrients in the small bowel; this will minimize nutrients available for colonic fermentation.

and are not universally tolerated by cats or dogs and should generally be avoided in animals with diarrhea when alternative options including intravenous or subcutaneous fluids are available.

Digestibility

Increasing the total digestibility of the diet can be beneficial in the treatment of both acute and chronic diarrhea as it reduces the amount of residual food being presented to the colon and, therefore, may reduce luminal bacterial overgrowth.[6] A highly digestible, low-fiber diet is often described as one with a protein, fat, and carbohydrate digestibility of ≥ 85–87%, 90%, and 90%, respectively.[7,8] Ingredient selection, processing (e.g., fine grinding), and cooking can alter total digestibility. Most veterinary therapeutic GI diets incorporate highly digestible and bioavailable protein sources such as egg and poultry by-product meal, as well as highly digestible carbohydrate sources such as rice and corn meal.[9]

Fiber

Fibers are carbohydrate compounds that are resistant to gastric digestion and intestinal absorption. Fibers can provide both a chemical effect through their interaction with resident intestinal bacteria and a physical effect that is mediated by water retention, volume distension, and promotion of intestinal motility through activation of stretch receptors. The interplay with body water demands that the patient be adequately hydrated prior to the use of fiber sources. The effect of fibers is dependent on their classification. Fibers can be classified as soluble or insoluble, viscous or non-viscous, and non-fermentable or fermentable compounds. Fermentable fibers typically also have prebiotic effects. Bacterial fermentation of fermentable fibers results in the production of short-chain fatty acids (SCFAs; i.e., acetate, butyrate, proprionate) and has the potential to confer a number of advantages to the host including supporting the growth and activity of the commensal intestinal microbiota (most commonly anaerobes such as *Bifidobacteria* and *Lactobacilli*), inhibiting the growth of pathogenic bacteria, providing an energy source for colonocytes, increasing antioxidant systems, increasing luminal water and electrolyte absorption, and reducing tissue inflammation. Additional benefits include stimulation of the immune system, production of vitamins, increased tissue sensitivity to insulin, and reduction of toxic metabolites such as bile acids.[10] The SCFAs are often decreased in critically ill patients, which has been associated with increased GI complications including dysmotility and diarrhea. Thus, supplementation with fermentable fibers may help to restore healthy microbiota and reduce the occurrence of these GI complications, especially in hospitalized animals with diarrhea. Insoluble fibers (e.g., cellulose) can increase fecal bulk whereas soluble fibers (e.g., psyllium) can help to draw in and absorb luminal water. Mixed fiber preparations with both soluble and insoluble fiber, such as those found in fiber-enriched gastrointestinal diets, have been demonstrated to be beneficial as a sole therapy for acute, large intestinal diarrhea.[3,11]

Fat

The decision to reduce the dietary fat fed to diarrheic animals is based on evaluation of the signalment, current clinical signs, and physical examination

findings. Digestion of fat requires emulsification by pancreatic lipases and colipase as well as the detergent action of bile acids. Once absorbed into the enterocyte, most fatty acids and monoglycerides, except for some medium-chain fatty acids, are repackaged as triglycerides into chylomicrons and delivered to the systemic circulation via the lymphatic system. Fat digestion and absorption can be compromised because of exocrine pancreatic insufficiency, hepatic or gallbladder dysfunction, injury to the intestinal brush border, or lymphatic dysfunction. In the absence of these conditions, the majority of cats, including those with diarrhea, are tolerant of high-fat diets.[12] Dietary fat should be reduced in animals with diarrhea in the presence of gastrointestinal motility disorders, steatorrhea, pancreatitis, hepatic or gall-bladder disease, hyperlipidemia, or lymphangiectasia. However, as fat is the most energy dense macronutrient, maintaining a moderate amount of fat in the diet, when possible, should be considered to reduce food volume in animals with evidence of volume intolerance or those that are underconditioned. Altering the fat composition to reduce saturated fats and enrich the diet with the omega-3 fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), may be beneficial to dogs, and likely cats, with chronic diarrhea.[13]

Protein and Amino Acids

Dietary protein not only provides essential amino acids and nitrogen but also serves as an important palatant for both dogs and cats. Dietary protein is categorized by its origin (e.g., plant, animal, insect), quality (e.g., amino acid composition, digestibility), amount, and form (intact, hydrolyzed, amino acid-based). Acquisition of a complete dietary history and evaluation of lean body mass, skin quality, total serum protein, and serum albumin provide non-invasive ways to interrogate the total body protein status and may help to determine the target for dietary protein. Protein digestibility is one of the most important considerations in animals with diarrhea. In animals with chronic diarrhea, particularly those with evidence of protein energy malnutrition, the amount of dietary protein, its form, and its quality (ratio of essential to nonessential amino acids) require special attention. In the presence of a severely diseased intestine such as with severe chronic inflammatory enteropathy, loss of villus surface area may lead to the inability to digest and absorb excess dietary proteins, resulting in osmotic diarrhea and colonic fermentation. Animals with concurrent cutaneous signs such as pruritus typically have immunologic reactions to protein. Thus, it may be prudent to feed these animals a diet with a moderate dietary protein concentration that includes protein in the form of a hydrolysate or that is comprised of individual amino acids in the initial stages of recovery. Specific amino acids such as glutamine also play a more important role in regulation of the gut mucosal barrier. Glutamine is a conditionally essential amino acid and is the preferred energy source for rapidly dividing cells such as enterocytes. Glutamine may improve intestinal permeability by stimulation of tight junction protein expression.[14] Oral glutamine is rapidly absorbed by the small intestine and less likely to have a beneficial effect on the colon. Currently, there are no published studies evaluating the effects of orally or parenterally administered glutamine in dogs and cats with diarrhea. These are needed before any recommendations regarding additional glutamine supplementation can be made.

Soluble Carbohydrates

Digestion of dietary soluble carbohydrates requires the presence of both luminal pancreatic amylases and an intact intestinal brush border expressing surface disaccharidases. In the author's experience, young kittens or animals chronically (i.e., years) eating a low soluble carbohydrate diet such as a raw food diet may have downregulation of pancreatic and intestinal disaccharidase activity and can develop diarrhea when quickly transitioned to a diet containing a large amount of carbohydrates. Additionally, cats, and rarely dogs, with chronic enteritis may develop diarrhea with diets containing a high proportion of carbohydrates, especially those containing improperly cooked or raw starches.[9] A trial with a high protein, low soluble carbohydrate diet (e.g., feline diabetic diet) should be considered in these cases.

Vitamins and Minerals

Animals with severe diarrhea, especially those with reduced food intake or malabsorptive diseases, are particularly at risk for vitamin and mineral deficiencies. For example, young dogs with parvovirus infection are prone to cobalamin (vitamin B12) deficiency.[15] The B vitamins including thiamine, riboflavin, pyridoxine, niacin, and cobalamin play an important role in the conversion of nutrients into energy. Thus, supplementation with B complex and cobalamin should be considered for any animal with prolonged

(> 3 days) hyporexia or anorexia. The impact of mineral supplementation outside of that contained in the enteral feeding in animals with acute diarrhea is unknown. However, in a study of young, orphaned kittens with diarrhea, those receiving a vitamin and mineral supplement were significantly more likely to survive whereas other treatments including a probiotic containing *Enterococcus faecium* SF68, metronidazole, or penicillin G had no effect on survival.[16] It was not possible to determine if the kittens benefited from the inclusion of additional vitamins, minerals, or both. Thus, more studies are warranted to determine what minerals, if any, would be beneficial in the supportive care of young and adult dogs and cats with diarrhea. In states of chronic diarrhea, especially those with protein-losing enteropathy, animals may benefit from cobalamin, folate, calcium, magnesium, and/or vitamin D supplementation.

Timing and Frequency of Feeding

Patients with early satiety or bloating, motility disorders, or malabsorptive diseases (e.g., protein-losing enteropathy, lymphoma, etc.) may benefit from multiple (≥ 3) small meals throughout the day. Adjusting moisture content in the diet can also help address issues related to dysmotility, volume intolerance, or increased fecal water.

MONITORING

Maintaining a daily log including notation of symptoms (e.g., bloat, vomiting, change in appetite, regurgitation, early satiety, abdominal pain) and their relationship to time of day and activities, including exercise and feeding, can be helpful to further characterize the disease and monitor response to nutritional and pharmacologic interventions. A fecal scoring system should be used as a qualitative assessment of fecal consistency.

BENEFITS OF MEDICAL VS NUTRITIONAL MANAGEMENT

Nutritional intervention is a relatively low risk solution that has the potential to have a dramatic impact in the treatment of acute or chronic diarrhea in both dogs and cats regardless of the origin. Even in animals without true adverse food reactions, nutrition plays an important role in resolution of intestinal inflammation and recovery. In many studies, nutritional interventions are as good or better in helping to improve fecal consistency compared with medical management such as antibiotics or probiotics.[11,17] As such, dietary therapies such as those mentioned above should be considered as the sole therapy or alongside pharmacologic approaches, unless a highly digestible gastrointestinal diet or high-fiber gastrointestinal diet is contraindicated due to other medical conditions. Medical management strategies for acute and chronic diarrhea include approaches or therapies to modulate the microbiome (e.g., probiotics, fecal microbial transplantation, antibiotics), immunomodulatory drugs, adsorbents, and bile acid sequestrants. These strategies along with studies demonstrating head-to-head comparisons, when available, are reviewed below or elsewhere.

COMMUNICATION TIP

Maintaining a daily log including notation of symptoms and their relationship to time of day and activities, including exercise and feeding, can be helpful to further characterize the disease and monitor response to nutritional and pharmacologic interventions.

Probiotics

According to the International Scientific Association for Probiotics and Prebiotics, probiotics are live microorganisms that, when administrated in adequate amounts, confer a health benefit on the host.[18] The combination of a probiotic with a prebiotic is known as a synbiotic. Most probiotics contain lactic acid-producing bacteria (LAB), as these tend to be decreased in inflammatory enteropathies, but yeast-containing probiotics are also available. In several studies, a substantial number of probiotics on the market for human or animal use did not contain the claimed organism, contained additional species including potential pathogens not listed on the label, or contained markedly lower concentrations than

stated on the label.[19,20] Thus, practitioners and clients should scrutinize probiotic products and only choose probiotics produced from trusted companies with good quality control measures and with evidence of the safety of the probiotic in the intended species. In studies of acute, idiopathic diarrhea, probiotics may slightly improve the time to resolution of diarrhea and increase short-chain fatty acid production;[2,21] therefore, probiotics or synbiotics may be reasonable adjunctive management tools or alternative options, especially when feeding a therapeutic gastrointestinal diet is not possible. With the exception of one uncontrolled study evaluating the use of probiotics for canine parvovirus infection,[22] the benefit of probiotic administration for infectious diarrhea in dogs and cats is unknown.

The results of probiotic administration on chronic diarrhea in dogs and cats are limited and mixed. Probiotics may improve the gut mucosal barrier and immune response; however, there does not appear to be a benefit to their use in animals with food-responsive diarrhea.[23] Therefore, a dietary trial is recommended prior to reaching for probiotics, especially if food-responsive diarrhea is suspected. In dogs with other forms of chronic inflammatory enteropathy, probiotic administration may improve the intestinal immune response and clinical severity.[24,25] There are not enough placebo-controlled, randomized clinical trials to determine if probiotics are beneficial for the treatment of chronic diarrhea in cats. The heterogenous effect of probiotics in the adjunctive treatment of chronic enteropathy are likely related to host factors (e.g., age, breed), environmental factors (e.g., diet, disease state), or probiotic factors (e.g., timing or route of administration, the type or concentration of probiotic bacteria administered). The efficacy of probiotics may also depend on good owner compliance and duration of therapy. For example, in one study of dogs with chronic enteropathy, investigators demonstrated that a *Saccharomyces*-containing probiotic had to be administered for 30–45 days before a significant difference could be observed compared to placebo.[25] Although more studies are needed, it is logical that a longer course of therapy would be required for a more chronic disease state as compared to an acute one.

Fecal Microbial Transplantation (FMT)

Microbial transplantation (i.e. transfaunation) has been performed for decades in large animal medicine. It has only been recently that microbial transplantation in the form of FMT has become popular for the treatment of diseases in small animals. FMT involves the administration of feces taken from a healthy donor and given to a diseased recipient with the goal of providing a physiological benefit to the host. Benefits of FMT administration may be due to the transfer of microbiota including bacteria, viruses, fungi, and protozoa or their microbial products. After preparation and dilution, the fecal sample is often delivered into the proximal duodenum via endoscopy or into the proximal colon via enema. More recently, at least one commercially available encapsulated FMT has been developed, but to the author's knowledge, there are no prospective placebo-controlled studies evaluating this orally administered product. In the context of acute diarrhea, FMT improved fecal consistency and hospitalization time in dogs with parvovirus infection.[26] The use of FMT therapy for acute diarrhea in dogs showed improvement in both fecal consistency and gut microbial health compared with metronidazole.[27] This study did not include a control group so it is difficult to determine if FMT provides a benefit when compared with provision of a highly digestible diet alone. In one study evaluating the benefit of FMT for dogs with chronic inflammatory enteropathy, the addition of FMT did not impart an effect in dogs already receiving prednisone and a hydrolyzed diet;[28] however, as with probiotics, it is likely that the beneficial effects of FMT are largely dependent on donor and patient selection, route of administration, and dosage. More studies are needed to determine when FMT should be recommended and how to screen donors; however, FMT should be used with caution in immunocompromised animals.

Antibiotics

Until recently, the use of antibiotics for the treatment of both acute and chronic diarrhea in dogs and cats was routine. Although antibiotics such as metronidazole or tylosin can help improve fecal consistency, they carry unacceptable side effects including negative alterations of the host microbial environment (i.e., dysbiosis) and increased frequency of multi-drug resistant infections in the case of metronidazole. Moreover, in head-to-head trials, highly digestible diets or fiber-enriched diets with or without synbiotic supplementation are just as effective or more effective than antibiotics for the treatment of non-septic acute diarrhea.[3,11,29–31] When antibiotics are warranted, such as in cases of septic conditions, the use of antimicrobial guidelines and hospital antibiograms are recommended.

Nutraceuticals and Adsorbents

Nutraceuticals have been described as foodstuffs that provide both nutritional and medical benefits. Regulation of nutraceuticals is potentially limited. Several zinc- or prebiotic-based nutraceuticals have been evaluated for use in human patients with diarrhea. Oral zinc supplementation is often given to diarrheic children in developing countries and has been demonstrated to improve the duration and severity of diarrhea.[32] The use of zinc for the treatment of diarrhea in dogs and cats is limited to two studies, both of which were investigating dogs with acute diarrhea. A supplement containing zinc-carnosine and vitamin E was not effective in reducing acute diarrheic events secondary to cyclosporine administration in dogs.[33] In another study, a zinc-containing synbiotic helped improved fecal consistency in dogs with acute diarrhea, but the beneficial effects of zinc alone, if any, were unable to be determined.[29] Decreased serum zinc is associated with increased disease severity in dogs with chronic enteropathy.[34] Thus, more studies are warranted to evaluate the effect of zinc alone and identify the appropriate dosage of zinc for the treatment of diarrhea in small animals.

Prebiotics are non-digestible, fermentable foodstuffs that serve as nutrients for intestinal bacteria. These include fructooligosaccharides, galactooligosaccharides, resistant starches, β-glucan, and polyphenols. Prebiotics have been demonstrated to reduce markers of oxidative stress and increase markers of gut health in dogs with chronic enteropathy; however, to date, there are no studies in which supplementation of prebiotics alone improved fecal consistency or other measures of clinical disease activity in dogs or cats.[35–37] This may be because many therapeutic gastrointestinal diets already contain prebiotics.

Adsorbents including kaolin, pectin, bismuth subsalicylate, and clays are also commonly administered for the treatment of acute diarrhea in dogs and cats.[38] To the author's knowledge, there is only one study evaluating their efficacy without the concurrent administration of prebiotics and probiotics. Smectite clay, a natural aluminosilicate clay, improved chemotherapy-induced diarrhea in dogs.[39] As with fiber supplementation, ensuring the patient is adequately rehydrated prior to the use of adsorbents is recommended.

Bile Acid Sequestrants

Bile acids undergo hepatic synthesis from cholesterol and in dogs and cats are conjugated to taurine prior to excretion in the bile, where they facilitate the digestion and intestinal absorption of dietary fats. In the healthy gut, approximately 95% of synthesized bile acids are actively reabsorbed in the ileum. The remaining 5% are deconjugated and dehydroxylated by colonic bacteria to form secondary bile acids and are passively reabsorbed by the colon or lost in the feces.[40] *Peptacetobacter* or *Clostridium hiranonis* is considered to be the most important bacteria in dogs and cats for the conversion of primary to secondary bile acids. Bile acids can stimulate fluid secretion and regulate colonic permeability and motility. Bile acid malabsorption (e.g., chronic inflammatory enteropathy, ileal resection) or failure of bile acid conversion (e.g., intestinal dysbiosis) may lead to increased colonic motility, secretion, and inflammation. Bile acid diarrhea is a relatively new concept in veterinary medicine but is a well-recognized complication in humans with a variety of intestinal, pancreatic, and gallbladder diseases whereby a variety of tests are available to help diagnose the condition. Decreased secondary bile acids have been observed in dogs with chronic enteropathy and exocrine pancreatic insufficiency.[41] Clinical signs of bile acid diarrhea may include abdominal cramping, fatigue, fecal incontinence, increased fecal fat and volume, and altered colonic transit. Treatment for people with bile acid diarrhea is dependent on the underlying cause and may also include feeding a reduced fat diet and administration of bile acid sequestrants (i.e., cholestyramine, colestipol, colesevelam).[40] At the time of this writing, a single case series exists evaluating the efficacy of bile acid sequestrants for the treatment of suspected bile acid diarrhea secondary to chronic enteropathy in dogs where cholestyramine was successful in normalizing fecal consistency in both cases.[42] More studies are needed regarding the long-term efficacy and safety of bile acid sequestrants in dogs and cats prior to specific recommendations for the use of this class of drugs in dogs and cats with diarrhea.

Immunomodulatory Drugs

Dogs and cats with chronic inflammatory enteropathies that fail dietary therapy may benefit from immunomodulatory drug therapy including glucocorticoids (prednisolone, budesonide) and/or other immunosuppressive drugs such as cyclosporine

or chlorambucil.[43–46] The use of immunomodulatory drugs must be weighed against the potential for adverse effects including increased risk for opportunistic infection, orthopedic injury, hypercoagulability, and muscle wasting. A thoughtful and systematic approach to dietary intervention is recommended prior to reaching for this class of drugs, especially in animals with a good appetite. Animals with a poor appetite and in whom an enteral feeding tube is not an option may also benefit from a low dose of prednisone or prednisolone to help increase appetite during dietary trials.

CONCLUSION

No matter the duration, the localization, or the underlying etiology, dogs and cats with diarrhea benefit from targeted nutritional interventions. Using available tools, including diet history forms and fecal scoring charts, practitioners should localize the origin of disease, identify concurrent clinical signs, and evaluate the effect of previous dietary interventions. In the absence of sepsis or other indicators of infection, antibiotics should not be used as a front-line therapy in dogs and cats with diarrhea. Nutritional interventions are often as good or better in helping to improve fecal consistency compared with medical management such as antibiotics or other management options such as probiotics. As such, dietary therapies should be considered as the sole therapy or alongside pharmacologic approaches.

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ACUTE VOMITING & GASTROENTERITIS IN DOGS & CATS

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KEY TAKEAWAYS

- Acute gastroenteritis is a diverse syndrome encompassing patients with mild, self-limiting to severe, life-threatening disease. A thorough clinical and nutritional history provides the foundation for appropriate management.
- Nutrition is a component of a multipronged treatment approach, which also addresses the underlying cause of illness, hydration, and pain control.
- Clear communication with the client is key to treatment success, particularly in the many cases managed on an outpatient basis.

OVERVIEW

Acute gastroenteritis is one of the most common reasons for pets to be presented to their veterinarian, comprising about 26% of canine and 32% of feline claims to a U.S. pet insurance agency.[1] Vomiting, change in stool form and/or frequency, and reduced appetite are the typical clinical signs which set the stage for malaise, dehydration, and potential hypovolemia. A myriad of conditions cause acute vomiting and gastroenteritis in dogs and cats, many of which will not be definitively diagnosed given the self-limiting nature of signs and confines of investigative tools. Considerations include mechanical obstruction, infectious disease (including parvovirus in dogs, or panleukopenia and feline infectious peritonitis in cats), acute pancreatitis, adverse food reaction, and toxin ingestion.[2,3] Cats are notorious for vomiting hairballs; they may also vomit secondary to constipation. Acute gastrointestinal (GI) upset can occur in either species secondary to numerous extra-GI disease processes such as uremia, cholangitis, endocrinopathy, or neurologic disease. Once specific causes for acute GI signs have been ruled out, nutritional therapy rises to the top of the heap of management strategies.

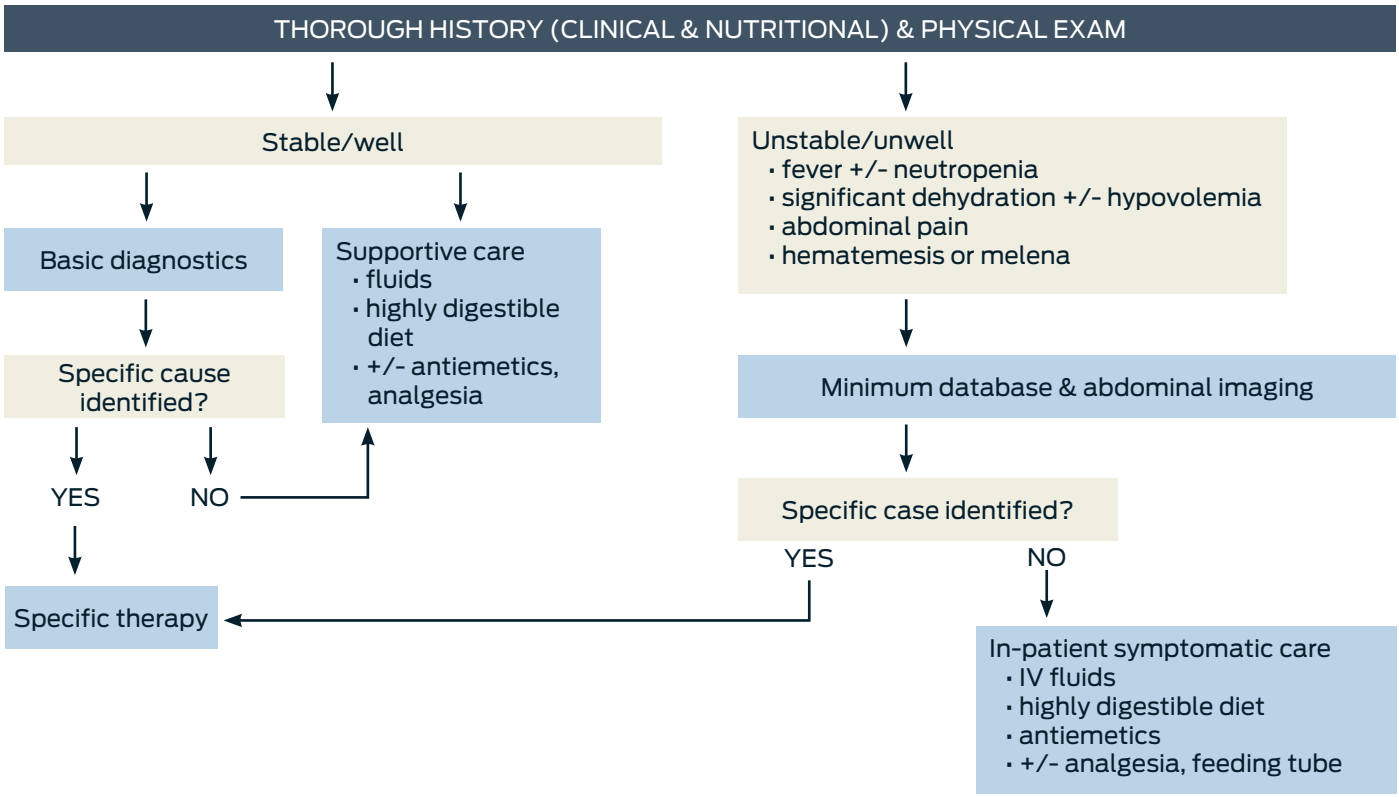
CLINICAL APPROACH

A thorough history is of paramount importance in the approach to acute gastroenteritis. Conversation with the client enables accurate characterization of clinical signs (e.g., distinguishing vomiting from regurgitation), which streamlines subsequent tests and treatment selection. Clients should be questioned regarding their pet's environment (e.g., the introduction of a new toy or plant, other pets in the household), frequency of defecation, vomiting, and/or regurgitation. Cat owners should be probed regarding the passage of hairballs and for abnormal litter box behaviors. In some cases, historical features point to a cause for the acute clinical signs (e.g., destruction of a toy, ingestion of a holiday meal). In others, more long-standing issues will be uncovered, or no obvious underlying cause will be revealed.

In addition to the clinical history, the nutritional history must also be addressed. This allows the care team to understand the patient's habitual diet (including supplements and treats), appetite, and eating style (e.g., meal-fed vs. grazer). It may also reveal a likely cause for signs (e.g., raw diet feeding, pica, counter-surfing, ingestion of wildlife or their remains). Open-ended questions beginning with "tell me..." may elicit more useful information compared with those starting with "what."[4]

Physical exam with particular attention to vital parameters, hydration status, and abdominal palpation (noting pain, peritoneal effusion, and/or mass effects) may further refine the problem list and helps identify unstable patients. An oral exam, including a survey beneath the tongue, should be completed given the propensity of cats to have linear foreign bodies anchored there.

Figure 1. Clinical approach to acute vomiting & gastroenteritis



DIAGNOSTIC CONSIDERATIONS

Following a complete history and physical exam, a problem list is devised, which enables the generation of differential diagnoses and an appropriate diagnostic plan (**Figure 1**). Stable patients may not require extensive workup; point-of-care testing including packed cell volume, total solids, electrolytes, blood glucose, and urine specific gravity may suffice. Red flags, including the presence of a fever, neutropenia, marked dehydration with or without hypovolemic shock, and/or hematemesis or melena, suggest the need for a more involved workup. Abdominal radiographs are indicated in many vomiting patients, with the primary purpose of ruling out mechanical obstruction. A complete blood count, chemistry panel, and urinalysis are of great help in ruling out extra-GI causes of acute gastroenteritis. Acute non-specific gastroenteritis is ultimately a diagnosis of exclusion; it is a reasonable differential given a short duration of signs and lack of red flags on initial assessment.

THERAPEUTIC PRINCIPLES

The therapeutic approach to patients with acute gastroenteritis is necessarily multipronged, simultaneously correcting fluid deficits, halting ongoing emesis, and controlling pain. Nutritional therapy is layered over these goals to generate a comprehensive treatment strategy to nurse the gut back to health.

Fluid therapy is critical to restoring normal GI tract function, and should be approached in terms of resuscitation, replacement, and maintenance phases. Patients with GI fluid losses are likely to be dehydrated, meaning their intracellular and interstitial fluid compartments are depleted;[2] as there are no specific, accurate tests for hydration, this must be estimated based on historical clinical signs and physical examination findings. Body weight is the most objective exam parameter and, when measured serially, is an excellent means of monitoring rehydration. Severe dehydration can lead to hypovolemia, meaning that the intravascular compartment is underfilled. The practitioner's assessment of the severity of dehydration and volume status will guide the most appropriate route of fluid delivery. Ranging from most stable to most critical, patients can be given fluids enterally, subcutaneously, or intravenously. Isotonic replacement crystalloid solutions are appropriate in most cases, in keeping with the mantra "*replace like with like*."

Medications may help reduce the severity of vomiting. The central antiemetic maropitant is effective in dogs[5] and cats.[6] One dose may be all that is needed to break the cycle of vomiting and simultaneously reduce nausea. If the patient appears to require an antiemetic for longer than a few days, further workup should be pursued to look for a root cause of vomiting. Oral bioavailability of ondansetron is <10% in dogs[7] and ~32% cats;[8] if prescribed, it should be given IV or SC.[9] Gastric acid reducers are rarely indicated in acute gastroenteritis. They should be reserved for patients with risk factors for GI erosion and ulceration.[10]

Medications are less reliable to rapidly resolve diarrhea unless a specific cause is identified (e.g., parasites). If frequent defecation negatively impacts the pet and/or client's quality of life, symptomatic therapy with loperamide or bismuth subsalicylate can be initiated. Loperamide should not be prescribed in cases where infectious enteritis is suspected (e.g., fever, bloody stools, ingestion of raw food) as rapid expulsion of gut contents might be a protective and necessary mechanism.[11] Although it is common practice for antibiotics to be prescribed to acute gastroenteritis patients, justification for this is poor. Acute gastroenteritis is rarely due to primary bacterial enteritis, and even in cases of acute hemorrhagic diarrhea syndrome, antibiotics have *not* been associated with more rapid recoveries or improved survival.[12] Oral antimicrobials disrupt the normal GI microbiome, which may not spontaneously recover after drug cessation.[13,14] Metronidazole has also been associated with reversible neurotoxicity (dogs and cats)and DNA damage (cats);[15] its strong metallic taste may cause ptyalism and food aversion. Although a study of 31 dogs with non-specific diarrhea given metronidazole had a mean 1.5-day quicker return to formed stool,[16] another study of 59 dogs with large bowel diarrhea found that the inclusion of metronidazole in the treatment plan was associated with a *longer* time to recovery.[17] Aspects of the individual patient, such as immune competence, complete blood count results, and vital parameters, should inform the decision to prescribe antimicrobials.

COMMUNICATION TIP

"Provided the diagnostic workup did not reveal a specific cause for gastroenteritis and no red flags were encountered, clients can be counseled that most causes of acute gastroenteritis are self-limiting."

Recent studies refute the once widely accepted practice of withholding food from acute gastroenteritis patients. The primary nutrients for enterocytes–glutamine and ketone bodies–come from the gut lumen, not the blood stream.[18] Moreover, many patients have already been anorectic for hours to days prior to presentation to their veterinarian. Fasting (specifically, lack of enteral nutrition) has been associated with reduced villus height and increased risk of bacterial translocation in dogs and humans.[19,20] Waiting 2 to 4 hours after the last bout of vomiting may be sensible. Strong evidence exists for the provision of calories enterally for canine acute pancreatitis (AP). Qin and colleagues[21] found no increase in serum amylase concentrations or pancreatic juice secretions in dogs after intrajejunal feeding, suggesting that enteral nutrition does not further exacerbate an inflamed pancreas. Moreover, AP dogs fed via esophagostomy tube had *lower* incidences of vomiting and regurgitation and no exacerbation of pain compared with parenterally fed patients.[22] Early initiation of enteral feeding via nasoesophageal tube in 15 parvovirus puppies was associated with a *shorter* median time to appetite recovery and cessation of vomiting and diarrhea.[23] While most cases presenting to the clinic will not ultimately be diagnosed with acute pancreatitis or parvovirus, we can extrapolate findings to less severely affected patients and aim to provide enteral nutrition as soon as possible.

Challenges arrive in patients that do not readily accept offered foods. Anorexia to hyporexia should prompt a reassessment of the patient (**Table 1**). Appetite stimulants should only be administered after other supportive therapies have been given time to work. Typically, anorexia is a sign that the disease has not been adequately managed and administering appetite stimulants before addressing the reason for lack of appetite can be problematic. Once other factors have been addressed (see Table 1), assisted feeding with a feeding tube is a more appropriate and likely more effective solution. While neonatal patients may tolerate syringe feeding, force-feeding is generally to be avoided.[24] Hospitalized patients may receive liquid

Table 1. Factors to consider in approaching an anorectic patient

Considerations	Examples	Further diagnostics & solutions
Uncontrolled pain	unidentified obstruction, pancreatitis	abdominal imaging, analgesia
Medication side effect	bitter tasting oral medication	administer subcutaneously (SC) or intravenously (IV)
Motility disturbance	cramping, ileus, constipation, mechanical obstruction	cisapride or metoclopramide, abdominal x-ray
Hydration status	dehydrated or fluid overload	revisit fluid plan
Environmental stress	cat housed above a loud dog, lack of hiding spot	improve housing
Electrolyte disturbances	hypokalemia	revisit fluid plan
Neophobia	offering only canned food when patient prefers dry	check with owner regarding patient preferences
Barriers to food intake	Elizabethan collar, high-sided food bowl	remove Elizabethan collar; use clean, shallow bowl

diets via nasoesophageal or nasogastric tubes, which are associated with low complication rates and can be placed without general anesthesia.[25] For patients predicted to need longer-term nutritional (with or without fluid) support, esophageal feeding tubes are preferred as they can accommodate a wider variety of diets and allow for outpatient management.

Particularly for patients with recent vomiting, it is prudent to initially offer small amounts of food (e.g., ¼ normal meal size, or 25% of resting energy requirements if hospitalized, throughout the day). If tolerated, another small meal can be offered 2 to 4 hours later. Division of the daily caloric allotment over 3 to 6 small meals may be continued during the recovery period. Patients can gradually transition back to their normal feeding regimen as their clinical signs subside.

NUTRIENT MODIFICATIONS

Acute gastroenteritis is a *syndrome* stemming from numerous inciting causes. Thus, no single diet will be appropriate for all patients. One should consider the macronutrient profile, palatability, and moisture content as a starting point. Gastrointestinal inflammation may impair digestive capacity, so a highly digestible (>85% protein digestibility and >90% fat digestibility; information available from pet food manufacturer) diet is preferable. The ideal macronutrient blend of protein, fat, and carbohydrate for dogs with acute gastroenteritis is yet to be determined. The author suggests a moderate to low-fat diet for dogs, but no studies exist to prove this benefit. For cats, who are obligate carnivores, fat restriction is likely not needed.[26] In fact, higher fat diets offer the benefit of greater caloric intake with lower food volume. Higher moisture foods are more likely to clear the stomach more rapidly,[27] which may be beneficial in vomiting patients and may simultaneously help maintain normal hydration status.

Supplemental fiber may help with diarrhea[17] and provide beneficial prebiotic effects. However, higher soluble fiber content is expected to delay gastric emptying, which could exacerbate vomiting.[28] Insoluble fiber reduces digestibility, which may be undesirable in the state of gastroenteritis. Fiber is therefore a nutrient to pay attention to and tailor to the individual patient.

Palatability is an important consideration, particularly for tentative eaters. Cats typically have strong dietary preferences, and their anorexia may be due to neophobia (aversion toward the unfamiliar);[24] this reinforces the importance of the nutritional history. Offering a specific diet in the hospital may also result in aversion to that diet when the patient has been discharged, especially in cats. Warming the food or mixing in flavored broth (without added harmful ingredients such onions or garlic) may help combat hyporexia. Attention should also be paid to food presentation; handfeeding may be

necessary early on. The food bowl should be cleaned regularly and placed where the pet can access it without interruption or competition.

Ultimately, there are many diets that can be effective in acute gastroenteritis. These include commercial (e.g., gastroenteric formulas) and complete and balanced home-prepared diets. Veterinary therapeutic gastroenteric diets can be expensive, and typically include chicken as the protein source (of note in patients with suspected adverse food reaction or food allergy). However, commercially available gastroenteric diets are complete and balanced and often contain nutrients thought to support gastrointestinal health, such as prebiotics. Home-prepared diets meanwhile will be more labor intensive for clients and must be properly formulated by a board-certified veterinary nutritionist to be complete and balanced if used long-term. This is less of concern if only fed for a few days, but variability in ingredients and preparation may make it difficult to make a clear dietary recommendation without a specific formulated recipe. The care team should work together with the client to evaluate each patient as an individual in developing an appropriate nutrition plan.

CLIENT EDUCATION POINTS

Setting oneself up for success involves providing realistic expectations to clients. Provided the diagnostic workup did not reveal a specific cause for gastroenteritis and no red flags were encountered, clients can be counseled that most causes of acute gastroenteritis are self-limiting. However, it may take several days for things to normalize. Clients should be provided with specific instructions regarding feeding, including how much to offer and how frequently; one study found clear instructions from the veterinarian to be associated with 7-fold improved odds of compliance.[29] A care team member should reach out to the client within 24 hours to ensure things are going in the right direction and to answer any questions. Patients should be seen again if signs are not improving within 72 hours or are worsening despite supportive care. Failure to improve may indicate a missed etiology or that out-patient supportive care is inadequate. Further diagnostics, as well as more aggressive treatments, are indicated in these patients.

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CHRONIC ENTEROPATHIES IN DOGS AND CATS

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KEY TAKEAWAYS

- Response to specific dietary strategies in dogs and cats with chronic enteropathy is highly variable. Therefore, nutrition should be tailored to each animal using trial and error to determine the most effective strategy.
- Various studies have shown that a clinical response to diet in dogs and cats with chronic enteropathy is usually observed within two weeks. Therefore, the new therapeutic diet should be fed exclusively for at least two weeks to determine the response.
- Most dogs and cats with chronic enteropathy can be transitioned back to their original diet without showing any signs of relapse. In one study, 21% of dogs, and in another study, 29% of cats with gastrointestinal signs relapsed on challenge.

DEFINITION

Chronic enteropathies describe a group of idiopathic diseases resulting in persistent or intermittent chronic gastrointestinal signs. Chronic enteropathies are commonly subclassified into food-responsive, antibiotic-responsive, or immunosuppressive responsive, depending on the response to treatment. Currently, food-responsive enteropathy represents the largest subgroup, comprising of approximately two-thirds of all chronic enteropathy cases presenting to a secondary or tertiary referral hospital in dogs[1-3] and likely also in cats.

PATHOPHYSIOLOGY

Although the exact etiology of chronic enteropathies is unknown, the pathophysiology is thought to involve the variable interplay between four key components: host genetics, gastrointestinal mucosal immune response, intestinal microbiota, and environmental risk factors, such as diet. Diet is thought to serve as a potential risk factor in disease pathogenesis, as well as a target for treatment in chronic enteropathy.

CHARACTERISTICS OF FOOD-RESPONSIVE ENTEROPATHY

Dogs with food-responsive enteropathy are younger than those with steroid-responsive enteropathy[1,2] and are more likely to have predominantly large intestinal signs.[2] Their clinical severity at the time of diagnosis is also generally the lowest;[1] however, this has not been consistently shown in all studies.[2] Moreover, dogs with steroid-responsive enteropathy had significantly lower mean serum albumin concentrations when compared with dogs with food-responsive enteropathy.[1] Finally, the outcome of dogs with food-responsive enteropathy was shown to be very good in the first year after diagnosis.[1]

Cats with food-responsive enteropathy have also been shown to be younger than cats with idiopathic inflammatory bowel disease and alimentary tract lymphoma.[4] Cats with suspected chronic enteropathy that were first prescribed hydrolyzed diets with concurrent antibiotics and/or glucocorticoids had higher odds of a poor response compared with those cats that first received the diet without these medications.[5] This suggests there is merit in trialing a hydrolyzed diet first as a sole therapy in cats with suspected chronic enteropathy, before resorting to antibiotic and/or glucocorticoid therapy for cases that respond poorly.

NUTRITIONAL ASSESSMENT

Assessment of Diet

An assessment of the diet will firstly help to determine if the animal is consuming enough energy and nutrients, as well as determine the need for assisted dietary intervention. Second, assessment of the diet just prior to or at the onset of gastrointestinal signs may help to

identify dietary triggers for the chronic enteropathy. Collection of a full diet history of currently and historically fed diets, including snacks, treats, table foods, and foods used to administer medication will allow the compilation of a complete antigen exposure list, which can then be used to determine ingredients that would be novel for the animal.

An assessment of the fiber and fat content of the current and previous diets and the effect of these on the gastrointestinal signs will help to determine what strategies should be trialed next. For example, if a dog with colitis is already consuming a high-fiber diet with no improvement in diarrhea, then a diet with lower fiber and therefore higher digestibility (generally fiber and digestibility are inversely related) might help to improve clinical signs. Similarly, if a low-fat diet has already been trialed with minimal effect on gastrointestinal signs, restricting selection of a therapeutic diet to one that is also low in fat may not necessarily be needed.

Assessment of Animal

Assessment of the animal should include body weight, as well as trends, size, body condition score using the 9-point scale, muscle condition, and fecal scores. Specific assessment of the hair coat, foot pads, and ocular, cardiovascular, neurological, and skeletal systems are also important to assess the overall nutritional status of the animal.[6]

Although there are currently no laboratory tests that definitively assess the nutritional status of the animal, a minimum database comprising a complete blood count, serum biochemistry with electrolytes, urinalysis, and serum cobalamin and folate will likely help to provide additional insights into the nutritional health of a dog or cat with chronic enteropathy.

KEY NUTRIENTS

Fat

Dogs with chronic enteropathy may have increased passage of fat into the colon due to reduced fat digestion. Increased passage of fat into the colon may result in dysbiosis, as well as induce colonocyte damage and fluid secretion. Therefore, fat is a key nutrient in chronic enteropathy in dogs and feeding a low-fat diet may help to counteract these changes. Dietary fat did not seem to affect the outcome of cats with chronic diarrhea.[7] Therefore, dietary fat may be less of a concern in cats with chronic enteropathy.

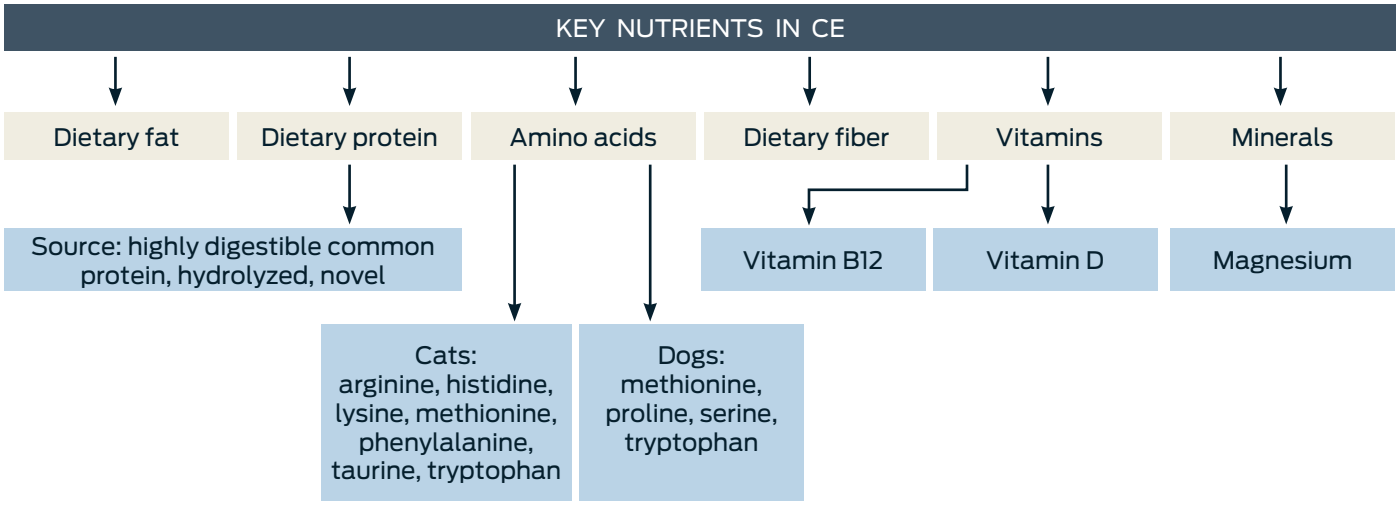
As low-fat diets may also help to increase gastric transit, animals with chronic enteropathy with nausea or vomiting may have an improvement in these clinical signs when fed low dietary fat.

Protein

The source of protein is important to consider when selecting a diet for dogs and cats with chronic enteropathy, as this may be the source of hypersensitivity or trigger of inflammation within the gastrointestinal tract. Protein sources in therapeutic diets intended for chronic enteropathy can be either:

- Highly digestible common protein, which reduces the amount of protein presenting intact to the gastrointestinal immune system due to high digestibility, but may contain potential antigens for dogs and cats with chronic enteropathy

Figure 1. Diagram of key nutrients to consider in canine and feline chronic enteropathies (CE)



- Hydrolyzed, which contains small peptides or amino acids thought to evade a type 1 hypersensitivity immune response by preventing cross-linking of two IgE antibody receptors on a mast cell
- Novel for the animal, which includes proteins the pet's immune system has not previously been exposed to and therefore should not elicit an immunological reaction

Unfortunately, at this time, further studies are needed to determine the optimum protein concentration for dogs and cats with chronic enteropathy.

Amino Acids

Cats with chronic gastrointestinal disease and dogs with chronic enteropathy have decreased plasma concentrations of amino acids (cats: arginine, histidine, lysine, methionine, phenylalanine, taurine, and tryptophan[8] and dogs: methionine, proline, serine, and tryptophan[9]). Also, plasma histidine and tryptophan concentrations were inversely correlated with severity of clinical signs in cats, and a negative correlation was seen between plasma serine concentration and clinical activity index in dogs.[8,9] Studies are needed to determine if supplementation with specific amino acids in dogs and cats with chronic enteropathy helps to improve clinical signs and disease outcome.

Fiber

Fiber can be classified based on its solubility in water, its viscosity, and its fermentation, with its action depending on these three properties. Solubility refers to the ability of the fiber to be fully dispersed when mixed with water. Fibers with increased viscosity can reduce the rate of passage of digesta through the gastrointestinal tract, slow down the rate of digestion of nutrients, and increase satiety leading to decreased food intake.[10] Fiber can also be described as rapidly to slowly fermentable. Fibers that are more rapidly fermented result in more short chain fatty acid (SCFA) production in a shorter period of time versus fiber sources that ferment more slowly. SCFAs can have numerous beneficial effects within the gastrointestinal tract.

Although a relatively small number of studies have assessed the effects of dietary fiber in canine and feline chronic enteropathy, high-fiber diets have anecdotally been shown to be beneficial for dogs and cats with chronic enteropathy with predominantly or exclusively large intestinal signs. Dietary fiber is thought to be effective in these cases due to its ability to:

- modify gastric emptying by altering the viscosity of ingesta
- normalize intestinal motility
- optimize intestinal mucosal barrier function
- promote homeostasis within the colon via the generation of SCFA, which have anti-inflammatory effects
- provide a buffering effect on toxins
- bind excess water
- promote the growth of beneficial bacteria.[11,12]

However, not all animals with large intestinal signs may respond favorably to a high-fiber diet. Therefore, trial and error with this strategy is needed and should be prioritized for those animals where the large intestinal signs did not improve with a highly digestible diet, and especially before the use of empirical antimicrobials.

Vitamins

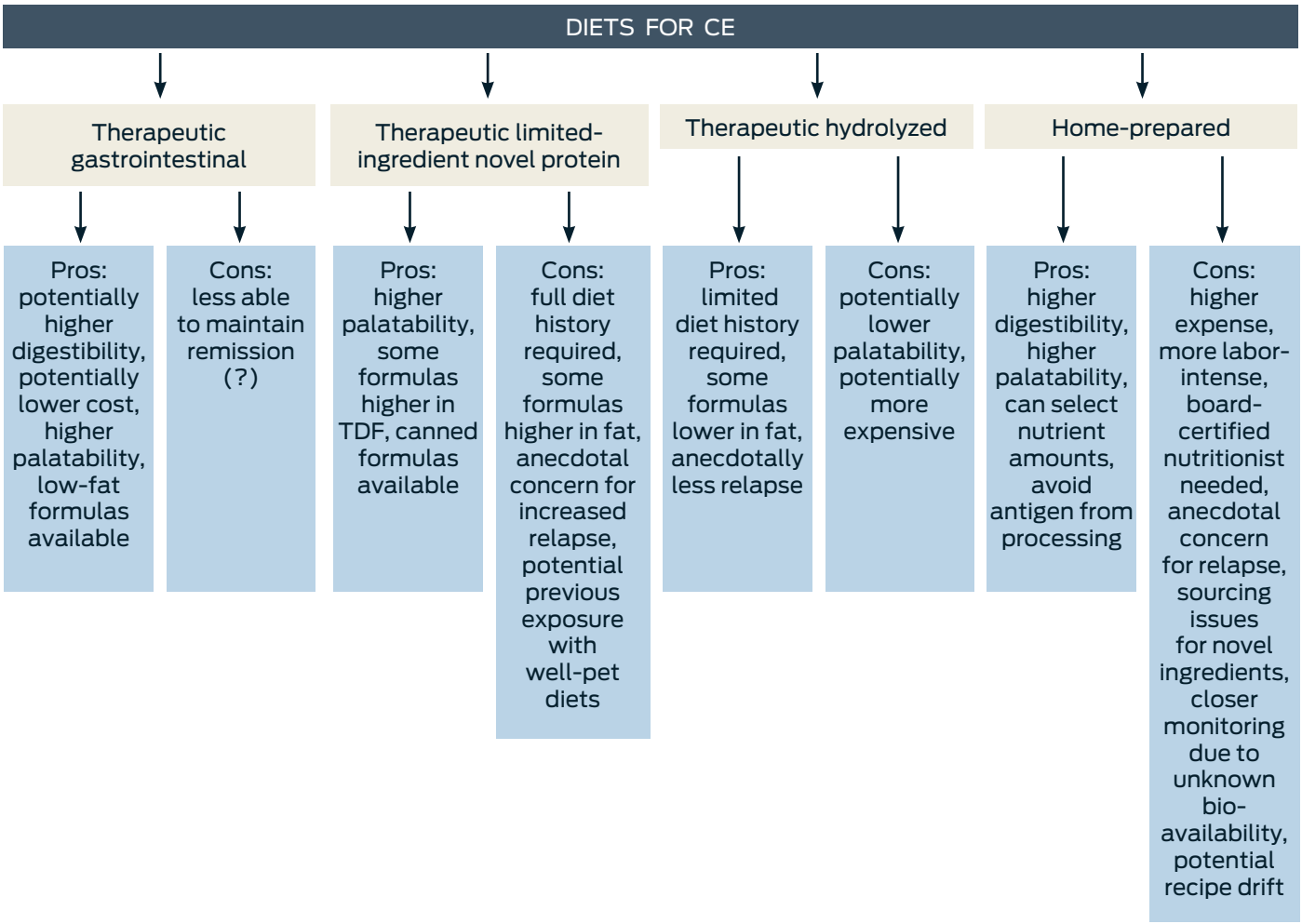
Several studies have shown hypocobalaminemia in dogs and cats with chronic enteropathy,[2,13] and this has also been shown to be a negative prognostic indicator in dogs.[2] Studies demonstrating the effects of oral cobalamin (vitamin B12) supplementation at normalizing serum cobalamin concentrations in dogs and cats have been reported.[14,15] Recommended doses for oral supplementation include 250 micrograms per day for cats and dogs below a body weight of 10 kg, 1000 micrograms for 10- to 45-kg dogs, and 2000 micrograms for dogs with a body weight above 45 kg. Cobalamin can also be administered subcutaneously.

Some dogs and cats with chronic enteropathy may have decreased serum vitamin D concentrations.[16,17] However, a consensus regarding vitamin D supplementation in animals with documented low concentrations has not yet been established.

Minerals and Other Micronutrients

Low blood magnesium concentrations necessitating supplementation may be seen in some dogs with advanced chronic enteropathy. Magnesium can be supplemented orally using a dose of 1–2 mEq/kg/day with either magnesium oxide, magnesium citrate, or magnesium sulfate. Supplementation may also be necessary in those cases with refractory hypokalemia

Figure 2. Pros and cons of diets used in the management of chronic enteropathies (CE) in dogs and cats (TDF = total dietary fiber)



or hypocalcemia. The most common side effect of oral magnesium supplementation is diarrhea.

Other micronutrient deficiencies such as zinc, selenium, and iron are known to be of concern in human inflammatory bowel disease,[18,19] but have not been investigated in canine or feline chronic enteropathy.

DIETARY THERAPY

Response to specific dietary therapeutic strategies in dogs and cats with chronic enteropathy is highly variable, which is likely due to the underlying genetic susceptibility and therefore pathogenesis, as well as environmental risk factors. Therefore, nutrition should be treated as an individualized therapeutic intervention with trial and error to determine the most effective strategy for each animal with chronic enteropathy.

Highly Digestible Gastrointestinal Diet

Some studies have shown that highly digestible therapeutic gastrointestinal diets can help with clinical signs of chronic enteropathy in both dogs and cats.[20-22] However, it is important to note that one study showed that although a highly digestible therapeutic gastrointestinal diet was able to induce remission in dogs with chronic enteropathy, they were less likely to remain asymptomatic at subsequent rechecks when compared with dogs managed with a hydrolyzed diet.[23]

Hydrolyzed Protein Diet

Hydrolyzed protein diets have been shown in multiple studies to be effective in the management of chronic enteropathies in dogs and cats.[1,23-27] These diets employ a number of strategies that might explain their effectiveness in chronic enteropathies. The hydrolyzed protein may help to influence the immune system, as well as increase digestibility. In addition, some

hydrolyzed formulas have a lower fat content and/or contain omega-3 fatty acids and soy, which are known to be immunomodulatory. Some hydrolyzed formulas are vegetarian, which may help to increase remission, as in people with inflammatory bowel disease.[28] Additionally, some hydrolyzed formulas are gluten-free, which in the author's experience may also be beneficial for certain animals even in the absence of wheat gluten hypersensitivity. Due to the scientific evidence and anecdotal success of hydrolyzed protein diets in canine and feline chronic enteropathy and the finding that some dogs that failed an elimination diet trial with a novel protein diet responded to a hydrolyzed protein diet,[26] these diets should likely be trialed first. If the animal does not consume the diet or the gastrointestinal signs do not improve, then a commercial therapeutic limited-ingredient novel protein diet can be tried.

COMMUNICATION TIP

"Response to specific dietary therapeutic strategies in dogs and cats with chronic enteropathy is highly variable, which is likely due to the underlying genetic susceptibility and therefore pathogenesis, as well as environmental risk factors."

Limited-Ingredient Novel Protein Diet

Nearly 50% of cats and 60% of dogs with chronic gastrointestinal signs respond positively to a novel protein diet.[29,30] One study showed no difference in response rates between hydrolyzed and limited ingredient novel protein diets in dogs with chronic enteropathy.[1] It is important to note that as one study demonstrated the presence of other common food antigens in well-pet novel protein diets, these diets should be avoided for the treatment of chronic enteropathies.[31] Some therapeutic novel protein diets may have higher total dietary fiber, and therefore these diets may be beneficial in those cases with large intestinal signs, especially if a highly digestible diet failed to improve the gastrointestinal signs.

Home-Prepared Diet

There may be a subset of dogs and cats with chronic enteropathies that may respond positively to a home-prepared diet rather than a commercial diet. Therefore, consultation with a board-certified veterinary nutritionist should be sought if the animal fails commercial therapeutic diets, so that a complete and balanced home-prepared diet can be formulated.

DIETARY INSTRUCTIONS

Feeding smaller meals more frequently throughout the day is advantageous in chronic enteropathies to prevent overloading of the gastrointestinal tract. If the animal has an ideal body condition, then the number of daily calories that were previously fed can be continued. If the animal is under-conditioned, the daily number of calories should be increased by 10% increments to offset any malassimilation from the chronic enteropathy until an ideal condition is reached.

A slow transition to the new diet should occur over 7 to 10 days, although in cats a longer period may be needed to help with acceptance. Various studies have shown that a clinical response to diet in dogs and cats with chronic enteropathy is usually observed within 2 weeks.[2,25,29,32] Therefore, the new therapeutic diet should be fed exclusively for at least 2 weeks to determine the response. The therapeutic diet should be fed exclusively, without additional treats or human foods.

Most dogs and cats with chronic enteropathy can be transitioned back to their original diet without showing any relapse. In one study, 21% of dogs and in another study, 29% of cats with gastrointestinal signs relapsed on challenge.[2,29]

REASSESSMENT AND MONITORING

Reassessment and monitoring are important after the new therapeutic diet has been initiated to ensure compliance and evaluate the effects, as well as to determine if any adjustments to the feeding plan are needed. The animal's body weight and body condition score should be monitored to ensure an ideal body condition is maintained or achieved with the new therapeutic diet. Appetite and food intake, overall appearance and activity, as well as gastrointestinal signs, including fecal scores should be regularly assessed and monitored.

Possible reasons for failure to respond to the new therapeutic diet include the need for a different dietary strategy or medication to control the clinical signs, owner non-compliance with feeding, concurrent diseases, or misdiagnosis of chronic enteropathy.

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PRACTICAL TOOL: DIAGNOSIS AND MANAGEMENT OF POTENTIAL GASTROINTESTINAL ADVERSE FOOD REACTIONS

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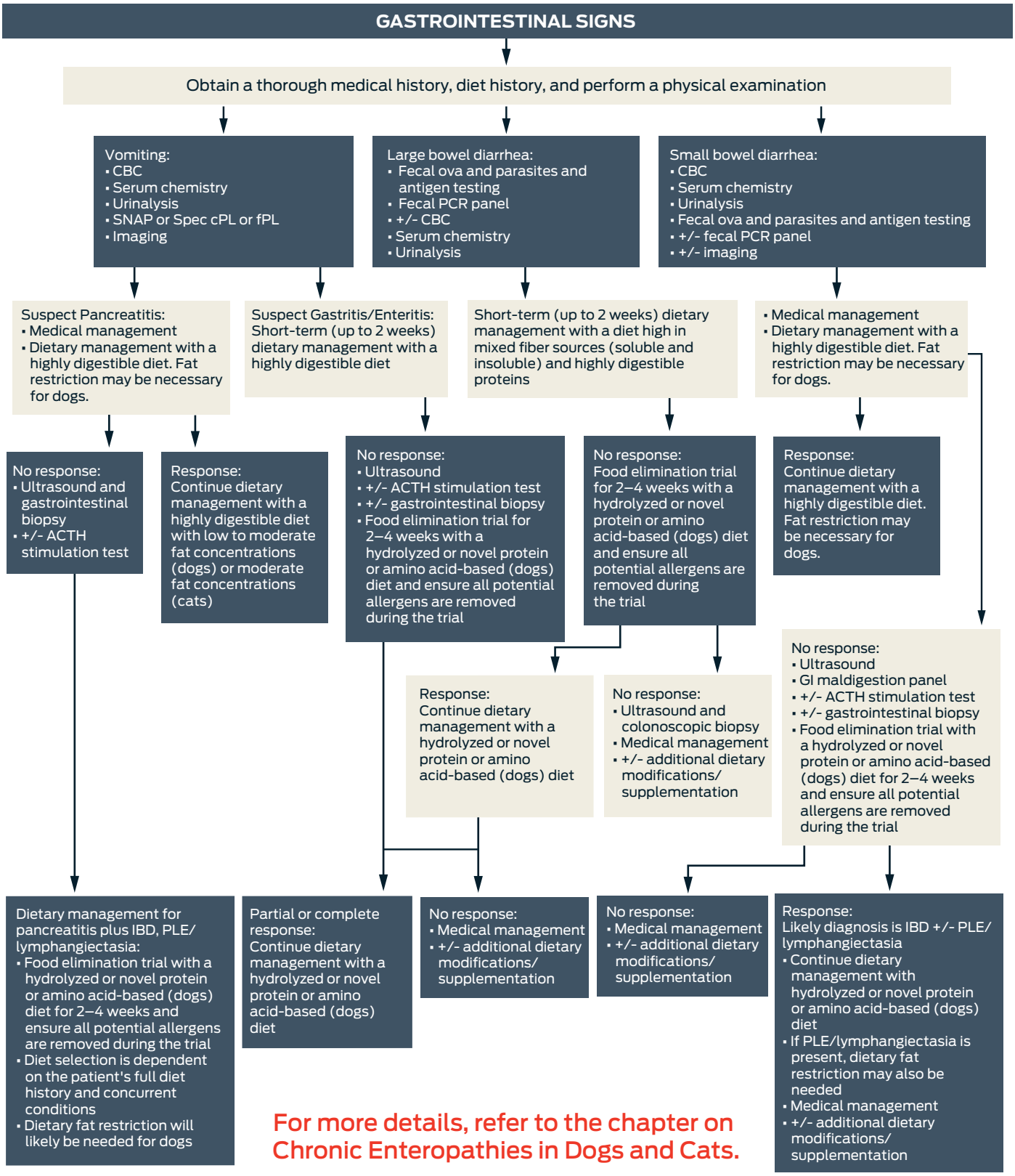

For more details, refer to the chapter on Chronic Enteropathies in Dogs and Cats.

PRACTICAL TOOL: UTILIZING FECAL MICROBIOTA TRANSPLANTS IN PRACTICE

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Fecal microbiota transplantation (FMT) is used to transfer feces from a healthy donor to a recipient with a disease in order to restore the intestinal microbiota and decrease disease activity. The transplant can be given orally as lyophilized feces in capsules, deposited in the duodenum using an endoscope, or administered rectally as a retention enema. Fresh or thawed frozen feces could be used for FMT. In people with recurrent *Clostridioides difficile* infection treated with FMT, frozen feces are as effective as fresh.[1] FMT is superior to antibiotic treatment in *Clostridioides difficile* infection in people, and appears effective in treating inflammatory bowel disease (IBD).[2-5] Fecal microbiota transplantation is a promising new treatment option in dogs with acute or chronic diarrhea.[6-12]

FMT IN COMPANION ANIMALS

FMT has been proven to significantly reduce time to recovery and hospitalization time in puppies with parvovirus infection.[7] Survival was higher in the FMT group compared with the control group, but the difference was not statistically significant. In another study of dogs with acute diarrhea, one FMT improved fecal quality to the same extent as seven days of metronidazole.[9] The FMT group had significantly improved fecal consistency and dysbiosis index (DI)[1] at day 28 compared with the metronidazole group.

In dogs with chronic diarrhea, a few case reports and one case series on successful FMT treatment have been published.[6,8,10,12] In the cases series, nine dogs with refractory IBD were included.[10] A significant decrease in canine IBD activity index (CIBDAI)[13] was seen after FMT. In a recent abstract on FMT treatment of 33 dogs with poorly responsive chronic enteropathy, clinical improvement was noted in 24/33 dogs after FMT, mainly expressed as increased activity level and/or improved fecal quality.[11] The dogs were treated with one to five FMTs (median three) as adjunctive therapy. CIBDAI decreased significantly after treatment.

In cats, only one case report is available. The cat had refractory colitis, which was successfully treated with FMT.[14]

DONOR SCREENING, DOSE, AND PROCEDURE

Guidelines to perform FMT in small animals are lacking,[15] but the Companion Animal FMT Consortium is working on guidelines at the time of publication of this practical tool. The following recommendations are based on original work by Jennifer Chaitman and co-workers, and the author´s clinical experience.[9,11]

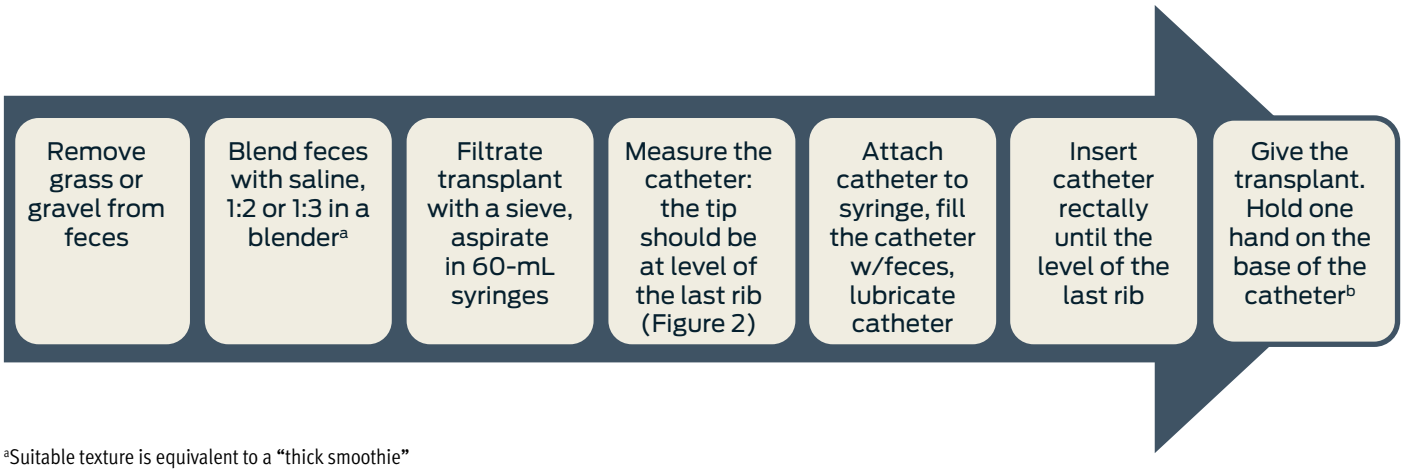
Donor Screening

Donors should be clinically healthy, not under treatment with long-term medications, with a normal body condition score and a CIBDAI of 0–3. Standard serum biochemistry and hematology parameters should be within reference intervals, and donors should not have been treated with antibiotics for a minimum of 6 months or fed a raw food diet. Donor feces should be free of fecal parasites, *Salmonella* spp., and C*ampylobacter jejuni*. To ensure high levels of beneficial microbes, donors are preferably screened with DI.[16,17] In people, the microbial composition and diversity of the donor stool is vital for successful treatment.[18,20]

Preparations and Dose

On the day of the procedure, food should be withheld from the recipient for 6 hours prior to FMT. Just prior to the procedure, the recipient should be walked for 30–40 minutes in order to defecate. FMT can be given without sedation, but the author often uses a low dose of acepromazine in dogs and full sedation in cats. This improves relaxation and may increase retention time after the procedure. Blend 5 grams of feces/kg body weight (BW) of the recipient for recipients with a BW <30 kg, and 3 grams/kg BW for dogs >30 kg. For the remaining procedure, see **Figures 1** and **2**. Different types of rectal catheters can be used. The author uses 16 French flexible suction catheters with atraumatic, rounded catheter tips for most dogs, and 14 French catheters for cats and miniature dogs. After FMT, instruct the dog or cat owner to drive home slowly and withhold food for 3–4 hours. Restrict dog walks to a

Figure 1. Step-wise approach on how to perform FMT, starting with preparation of transplant from donor stool



[a]Suitable texture is equivalent to a "thick smoothie"
[b]Holding a hand on the base of the catheter/syringe attachment prevents leakage and detachment

Figure 2. Measure the catheter prior to insertion. The tip of the catheter should ideally be placed at the level of the last rib.

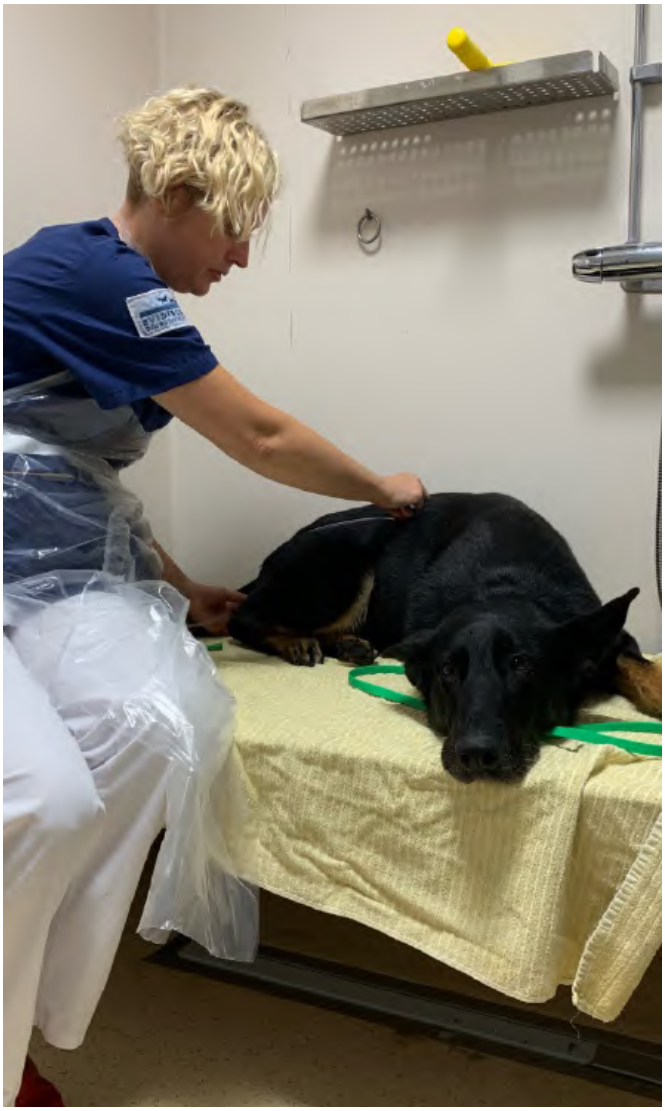


Photo by Linda Toresson, used with permission

minimum until the following day to prevent defecation and allow long contact time between the transplant and the colonic mucosa. Side effects are rare and self-limiting, but in some dogs, transient diarrhea, abdominal discomfort, or flatulence can be seen. A beneficial clinical effect of FMT can be seen within 1–14 days. For dogs with chronic enteropathies, recommend at least two treatments, preferably three, with 10- to 20-day intervals. The majority of dogs with chronic enteropathy in the recently published abstract showed further clinical improvement after the second FMT.[11] Repeated FMT has also been recommended in people with inflammatory bowel disease or *Clostridioides difficile* infection.[4,21-23]

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EXOCRINE PANCREATIC INSUFFICIENCY IN DOGS

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KEY TAKEAWAYS

- Exocrine pancreatic insufficiency (EPI) in dogs is diagnosed by a serum canine trypsin-like immunoreactivity (cTLI) concentration ≤ 2.5 µg/L.
- The majority of dogs with EPI are cobalamin deficient and cobalamin should be supplemented in any patient with a serum cobalamin concentration ≤ 400 ng/L (~ 295 pmol/L).
- Pancreatic enzyme replacement therapy (PERT) is the mainstay of management in dogs with EPI. Dietary management is also important and should be optimized for each patient individually. Most dogs with EPI respond to management and have a good quality of life and a normal life span.

INTRODUCTION

Exocrine pancreatic insufficiency (EPI) is a condition caused by insufficient synthesis and secretion of digestive enzymes by the exocrine pancreas.[1] Approximately 50% of dogs with EPI are German shepherds, which develop EPI due to pancreatic acinar atrophy (PAA), a condition that is believed to be hereditary and leads to almost complete atrophy of exocrine pancreatic tissue.[2] The remainder of patients can be dogs of any breed, which mostly develop EPI due to chronic pancreatitis. Key clinical signs of EPI are weight loss, a poor body condition score (BCS), and loose, voluminous stools with steatorrhea (**Figure 1A**).[3]

DIAGNOSIS

Clinical signs in dogs with EPI suggest a maldigestive disorder, which could result from severe small intestinal disease or EPI. Routine lab work (i.e., complete blood count, serum chemistry profile, and urinalysis) is mostly within normal limits in dogs with EPI, but in severe cases hypoalbuminemia maybe present. Serum concentrations of both lipid- and water-soluble vitamins are often decreased in EPI, although, with the exception of hypocobalaminemia, the significance of this finding is yet unclear.[4,5] Serum folate concentration can be increased in dogs with EPI, which is suspected to occur secondary to small intestinal dysbiosis.

The diagnostic test of choice for dogs with EPI is the measurement of serum canine trypsin-like immunoreactivity (cTLI) concentration.[6] The assay measures trypsinogen, trypsin, and some trypsin bound to protease inhibitors, hence the name "trypsin-like" immunoreactivity.[6] Also, the assay is highly species-specific and thus only assays for canine TLI (cTLI) can be used. In healthy animals, a small amount of trypsinogen leaks into the vasculature rather than being secreted into the pancreatic duct system. In contrast, this amount is severely decreased in dogs with EPI, leading to a serum cTLI concentration of ≤ 2.5 µg/L (also recorded as 2.5 ng/mL; reference interval at the GI Lab at Texas A&M University: 5.7–45.2 µg/L). It must be noted that many dogs with small intestinal disease have serum cTLI concentrations that are slightly below the lower limit of the reference interval, and thus only values ≤ 2.5 µg/L should be interpreted as being diagnostic of EPI. The test is considered to be both highly sensitive and specific.[6] Dogs with a serum cTLI concentration below the lower limit of the reference interval, but above the cut-off value for EPI, should be carefully evaluated for other differential diagnoses (mainly small intestinal disease). If no other potential causes for the clinical signs can be identified, the patient should be treated for possible EPI and a serum cTLI concentration should be re-evaluated in 3–4 weeks.

In Europe, fecal elastase has been marketed for the diagnosis of EPI.[7] The assay measures pancreatic elastase in feces, which is decreased in dogs with EPI. However, many dogs with a very low fecal elastase concentration do not have EPI and instead have small intestinal disease.[8] Thus, a diagnosis of EPI based on a

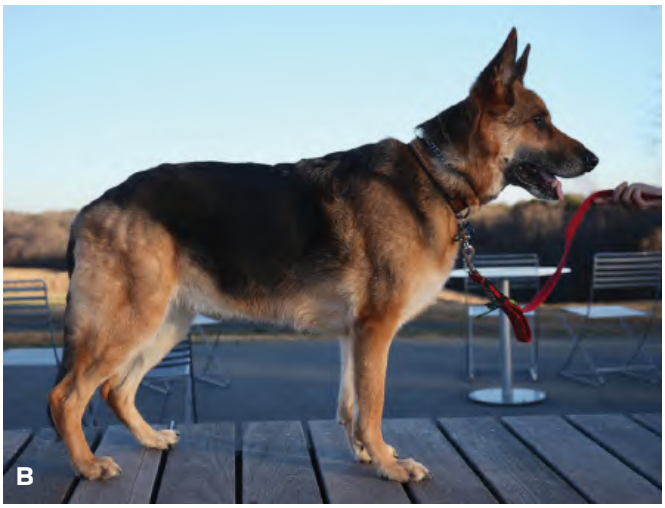


Figure 1. A, Dog with exocrine pancreatic insufficiency (EPI). The dog (Ziska) shown in this image was emaciated when rescued by her new owner. She had loose voluminous stools, a poor hair coat, and a poor body condition (BCS 1/9). Ziska was diagnosed with EPI and was successfully treated with PERT (B). Used with permission from Donna and William Warner and EPI4dogs.com.

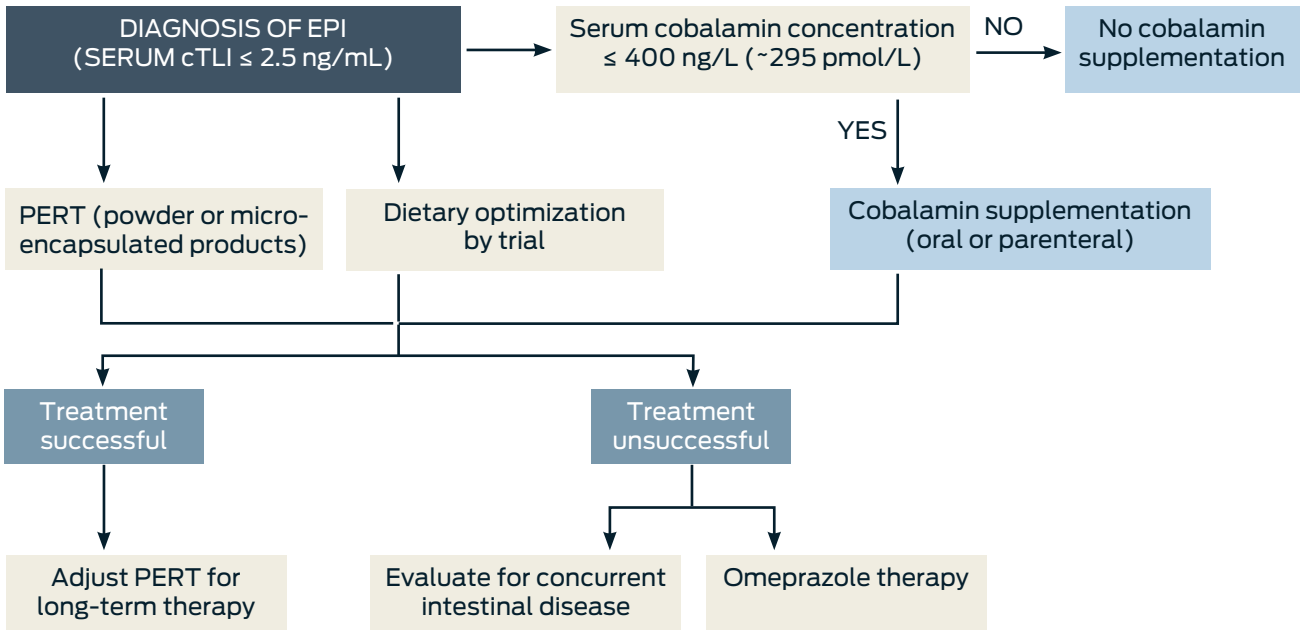
decreased fecal elastase concentration must be verified by measurement of serum cTLI concentration.

Other diagnostic tests, such as fecal proteolytic activity, should be avoided as they are frequently associated with both false positive and false negative test results.

MANAGEMENT

The mainstay of management of EPI (**Figure 2**) is pancreatic enzyme replacement therapy (PERT). A wide range of products are available (for an exhaustive list of products, as well as a wide range of information for pet owners, visit EPI4dogs.com). The rate-limiting component of PERT is lipase activity, thus care should be taken that the product contains sufficient amounts of lipase and the starting dose of the product should be adjusted when products that contain lower amounts of lipase are to be used. In general, powder is the preferred option for PERT, with capsules and tablets often failing to show efficacy. In Europe, microencapsulated products are frequently being used, which dramatically decreases the dose needed. When using such products, the capsule should be opened and the microencapsulated enzyme mixed into the food. Regardless of the formulation chosen for PERT,

Figure 2. Clinical management of dogs with exocrine pancreatic insufficiency (EPI)



the product should be mixed into the food, but pre-incubation is not necessary and results in malodor that may reduce owner compliance. A good starting dose is approximately 7,000 USP/kg (note that USP units are used in the USA, while other units such as Ph Eur U or BP U may be used in other countries, but the lipase potency of these different units is equal) of lipase or 1 teaspoon of PERT product per 10 kg body weight per each meal. It is crucial to note that this starting dose is often a lot higher than the ultimate maintenance dose, which can be adjusted to the lowest effective level once the patient has fully responded. In circumstances where PERT is not an option due to cost, availability, or other reasons, it should also be noted that raw pancreas from any species can also be used for PERT, although there are risks associated with feeding raw animal products, including food safety concerns. Pancreatic tissue should be chopped finely and frozen in portions per each meal. Approximately 50–100 g of pancreas should be used per 10 kg BW as a starting dose. To minimize the risk of exposure to pathogens from consuming raw animal products, care should be taken to procure pancreas from a reliable source and follow good hygiene practices when transporting, handing, and storing the material.

COMMUNICATION TIP

"Most dogs with EPI can be well managed long-term, have an excellent quality of life, and have a normal life-expectancy."

As mentioned, most dogs with EPI develop deficiencies in both fat- and water-soluble vitamins.[5] Deficiencies in fat-soluble vitamins are usually subclinical in dogs with EPI, and no clinical syndromes have been attributed to such vitamin deficiencies. However, a bleeding diathesis may rarely develop, and dogs that show bleeding tendencies should be carefully evaluated for a vitamin K-dependent coagulopathy and should immediately be supplemented with vitamin K until this diagnosis can be excluded. In contrast to fat-soluble vitamins, cobalamin deficiency, which has been reported to occur in 82% of dogs with EPI, can lead to many systemic clinical signs such as peripheral neuropathies, central neuropathies, immunodeficiencies, and/or anemia.[9] It may also lead to gastrointestinal signs and may be associated with treatment failure of PERT. Thus, serum cobalamin concentration should be measured in every dog diagnosed with EPI, and cobalamin should be supplemented in every dog with a serum cobalamin concentration that is less than 400 ng/L (~ 295 pmol/L), which is still well within the reference interval. This treatment recommendation is based on the fact that measurement of serum cobalamin concentration is not an ideal diagnostic indicator for cobalamin deficiency on a cellular level. Other parameters, such as serum methylmalonic acid, may be superior, but are technically demanding and expensive to measure, and thus not routinely available.[10] Cobalamin can be supplemented using cyanocobalamin (which is most commonly used), hydroxocobalamin, or methylcobalamin and can be given orally or parenterally. A recent study demonstrated similar efficacy for both, regardless of the underlying etiology.[11] Parenteral supplementation consists of 6 weekly injections (roughly 20–40 µg/kg BW), one more injection a month later, and reevaluation of serum cobalamin concentration a month later. Oral supplementation consists of daily supplementation (roughly 20–30 µg/kg BW) for 120 days with reevaluation 3–4 weeks after the last dose. If serum cobalamin concentration at the time of reevaluation is at the very upper limit of the reference interval, cobalamin supplementation can be discontinued. However, many dogs with EPI require lifelong supplementation. This may also be achieved by using a PERT product that contains cyanocobalamin.

There is no specific diet that is optimal for every dog with EPI, but instead the choice of an optimal diet needs to be individualized.[12] A good starting point is a highly digestible diet with a moderate dietary fat concentration as those diets often contain prebiotics—such as inulin or fructooligosaccharides—that will support the physiologic microbiota, which is disturbed in most dogs with EPI.[13] However, such a diet may not be optimal in all patients and if the management result is suboptimal, another diet should be trialed.[12] Other types of diets that may be trialed include elemental diets, hydrolyzed protein diets, or even maintenance diets. In humans, there are some initial trials using food that contains enzymatically modified fat, but such trials have not yet been conducted in dogs.[14] Diets that should be avoided include low-fat diets (on an energy

basis) and diets that are high in nonfermentable fiber, as the first may lead to malassimilation of essential fatty acids and the latter further impacts digestibility, which is not expected to return to normal even with PERT.[15]

If the treatment response using PERT, cobalamin supplementation (if serum cobalamin concentration was less than 400 ng/L (~ 295 pmol/L)), and various dietary trials is suboptimal, the patient should be carefully evaluated for concurrent small intestinal disease. Chronic enteropathy (CE) is very common in German Shepherds overall, and concurrent EPI due to PAA and CE does occur with some regular frequency. Also, similar to humans and cats, EPI due to chronic pancreatitis is also very commonly associated with CE in dogs of non-German Shepherd breeds. If concurrent intestinal disease is not identified, a trial with a proton pump inhibitor should be considered (e.g., omeprazole). Most PERT products utilize pork pancreas powder and thus unprotected pancreatic lipase, which is very susceptible to irreversible inhibition by the low pH in the stomach. Proton pump inhibitors have been shown to improve response to PERT in human EPI patients.[16] In very rare instances the fat content in the diet needs to be lowered, but this should be considered as a last resort as this is associated with negative consequences related to essential fatty acids and fat-soluble vitamins.

MONITORING

Monitoring of dogs with EPI involves monitoring fecal quality, body weight, and BCS. Assessing muscle condition score (MCS) can provide additional information on nutritional status. Repeated measurement of serum cTLI concentration is not useful, as the serum cTLI concentration is not affected by PERT and would be expected to stay diagnostic for EPI in most patients. Adjustment of PERT based on fecal quality is reasonable, as PERT in patients with a deterioration in fecal quality can easily be adjusted to improve fecal quality.

CONCLUSIONS

It should be noted that many dogs with EPI due to chronic pancreatitis can also develop diabetes mellitus, which needs to be managed appropriately. However, most dogs with EPI can be well managed long-term, have an excellent quality of life, and have a normal life-expectancy (**Figure 1B**). It is important to consider EPI in any dog with chronic gastrointestinal signs where another differential diagnosis is not apparent.

Finally, EPI is a life-long condition in almost all patients. But the pancreas does have some regenerative capacity and on occasion EPI does regress. However, this is rare and one should be careful not to elicit false hopes by the owner.

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LYMPHANGIECTASIA IN DOGS

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KEY TAKEAWAYS

- Intestinal lymphangiectasia is defined as the dilation of lymphatic vessels in the mucosa and/or submucosa of the intestine and is one of many causes of protein-losing enteropathy (PLE) in dogs.
- The main treatment strategies for intestinal lymphangiectasia include treatment of the underlying cause if identified, reduced dietary fat intake to help decrease fat absorption and intestinal inflammation, and symptomatic treatment for gastrointestinal signs.
- An improvement to a change in diet in dogs with protein-losing enteropathy is likely to be seen within 14 to 30 days, although many dogs require immunosuppressive medication in addition to dietary modification.

DEFINITION

Intestinal lymphangiectasia is defined as the dilation of lymphatic vessels in the mucosa and/or submucosa of the intestine and is one of many causes of protein-losing enteropathy (PLE) in dogs. Although intestinal lymphangiectasia overall is an uncommon disease in dogs, it is one of the most common causes of gastrointestinal protein loss. The definitive diagnosis of intestinal lymphangiectasia requires demonstration of intestinal lacteal dilation on histopathology.

PATHOPHYSIOLOGY

Intestinal lymphangiectasia can be congenital (primary) or acquired (secondary). Primary intestinal lymphangiectasia is considered to be uncommon in dogs. Acquired intestinal lymphangiectasia is most often due to intestinal, lymphatic, or mesenteric inflammation leading to increased pressure in lymph vessels. Primary neoplasia in the intestinal wall or mesentery, such as lymphoma or metastatic neoplasia in the mesenteric lymph nodes, could also cause acquired intestinal lymphangiectasia by obstructing lymph flow. Acquired intestinal lymphangiectasia can also result from diseases that increase venous hydrostatic pressure, such as right-sided heart failure. When pressure in the mesenteric or intestinal lymph vessels increases from inflammation, neoplasia, or increased venous hydrostatic pressure, the intestinal villous lacteals dilate, become more fragile, and rupture easily. Lymph then leaks from these ruptured lacteals into the intestinal lumen, resulting in the loss of all its contents, including chylomicrons, lymphocytes, and proteins (albumin and immunoglobulins). Some dogs with intestinal lymphangiectasia may also develop lipogranulomas, which are thought to be caused by a proinflammatory lipid substance present in the intestinal lymph.

CHARACTERISTICS OF INTESTINAL LYMPHANGIECTASIA

Although intestinal lymphangiectasia is primarily diagnosed in middle-aged dogs, it can affect dogs at any age. Similarly, although any breed can be affected, Basenjis, Norwegian Lundehunds, Rottweilers, Soft-Coated Wheaten Terriers, and Yorkshire Terriers appear to be predisposed.

CHARACTERISTICS OF FOOD-RESPONSIVE PROTEIN-LOSING ENTEROPATHY

One study demonstrated an optimal canine chronic enteropathy clinical activity index,[1] which is based on the presence and severity of nine factors including:

- attitude/activity
- appetite
- vomiting
- stool consistency

- stool frequency
- weight loss
- serum albumin concentrations
- ascites
- peripheral edema and pruritus

For each factor, a score is assigned based on the severity. A cut-off value of 8 distinguished the ultra-low-fat food-responsive PLE group (less than 8) from the immunosuppressant-responsive or non-responsive group (total score 8 or higher).[2] However, this finding was not replicated in other studies.[3] Studies have also demonstrated that dogs with food-responsive PLE have a better outcome compared with those requiring immunosuppressive medication.[3,4]

NUTRITIONAL ASSESSMENT OF THE ANIMAL

Malnutrition is prevalent in dogs with protein-losing enteropathy due to chronic enteropathy or lymphangiectasia. One study showed that two-thirds of dogs were under-conditioned and 88% had documented weight loss at the time of diagnosis with 32% having moderate weight loss (between 5 and 9.9%) and 43% having severe weight loss (at least 10%).[5] In addition, just under 50% of these dogs were hyporexic or anorexic at diagnosis.[5] This same study showed that 75% of dogs had decreased serum creatinine concentrations at the time of diagnosis, likely consistent with muscle loss. Given the high prevalence of reduced appetite, body weight loss, and decreased body condition score and potentially muscle condition in these dogs, assessment of these parameters to define the presence of undernutrition is paramount to determine if nutritional intervention is needed.

Although serum albumin, cholesterol, cobalamin, and folate concentrations at the time of diagnosis of PLE due to chronic enteropathy or lymphangiectasia were not predictors of mortality,[5] a minimum database including a complete blood count, serum biochemistry with electrolytes, urinalysis, and serum cobalamin and folate is important as part of the diagnostic investigation. In addition, the results may also help provide a gross overview of nutritional status.

KEY NUTRIENTS (FIGURE 1)

Fat

Low-fat diets help decrease chylomicron production, which is hypothesized to result in reduced lymphatic flow and pressure. This reduced flow and pressure then reduces lacteal dilation and rupture and subsequent loss of lymph. Indeed, dietary fat restriction, especially of long-chain triglycerides (LCTs), was associated with increased concentrations of serum albumin, less severe inflammation on histopathology, and resolution of clinical signs.[6,7] Furthermore, diets very low in fat may decrease lymph flow in the mesentery up to 10-fold compared with high-fat diets.[8] Also, as LCTs have proinflammatory properties and are hypothesized to cause lipogranulomas, reducing their intake may help reduce intestinal inflammation. Therefore, a low-fat diet is prioritized in the management of intestinal lymphangiectasia.

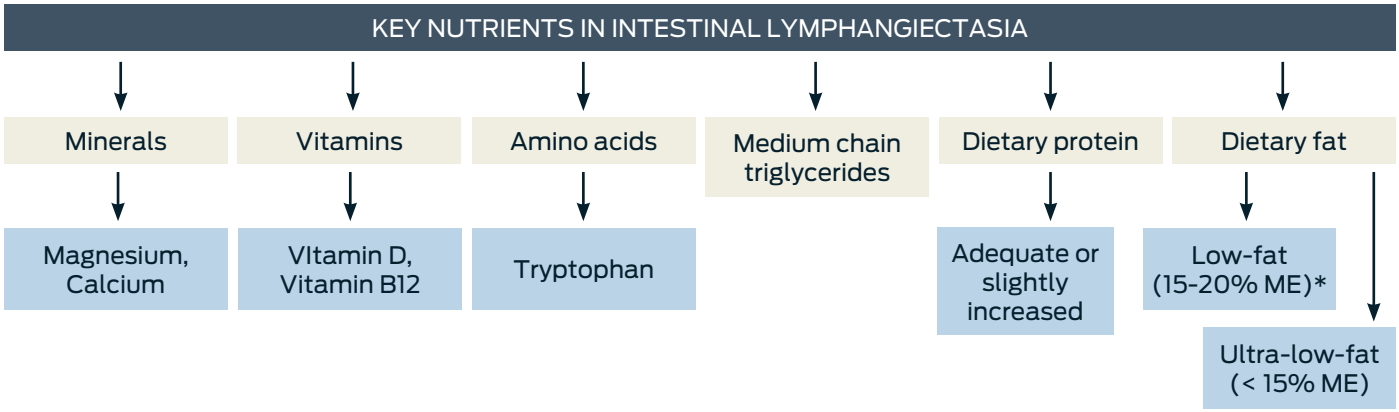
Medium-Chain Triglycerides

Medium-chain triglycerides (MCTs) are routinely added to the diet of humans with intestinal lymphangiectasia to increase the caloric intake without increasing lymph flow, as they are directly absorbed into the portal vein. However, one study in dogs showed that MCTs were still incorporated into chylomicrons and absorbed into the lymphatic system, therefore contributing to the composition of intestinally derived lymph.[8] Therefore, MCTs may not help reduce lymph flow when fed. However, MCTs are able to modulate intestinal inflammation and cause less damage than LCTs, as demonstrated in an animal model of ileitis.[9] Therefore, MCTs might help reduce inflammation in some dogs with intestinal lymphangiectasia while increasing caloric intake. Indeed, one dog showed

COMMUNICATION TIP

"It is not uncommon for these dogs to undergo trials with different successive diets utilizing different strategies before an adequate response is seen."

Figure 1. Diagram of key nutrients to consider in canine intestinal lymphangiectasia (ME = metabolizable energy basis)



* Highly digestible diets with a slightly higher fat content may be used with success in some patients and may be selected if a diet below 20% fat ME is not available. If concurrent diseases are present, such as secondary lymphangiectasia due to chronic enteropathy, this may necessitate selection of a specific diet strategy that results in a diet above 20% fat ME. In these cases, a diet in the chosen strategy with the lowest fat content should be selected.

good long-term outcome when fed a fat-restricted diet supplemented with MCTs.[10] However, in another study, dogs did not show changes in clinical status after 16 weeks of dietary supplementation with MCTs, but it is unclear whether the dogs were also fed a low-fat diet.[11] There is no consensus at this time regarding supplementation with MCTs and, therefore, the decision for their use should likely be made on a case-by-case basis. If MCT supplementation is used, assessment of clinical response should be based on improvement in gastrointestinal signs, body condition, and laboratory parameters such as serum albumin, globulin, cholesterol concentrations, and lymphocyte counts.

Protein

Although feeding an excessive amount of protein is not generally required in these cases, it is important to ensure that the animal receives an adequate amount of highly digestible protein, if not slightly increased above AAFCO and FEDIAF minimums, to help maintain muscle mass and restore serum protein concentrations to within the reference range.

Amino Acids

One study demonstrated that serum tryptophan concentrations were decreased in dogs with inflammatory PLE and that the concentration was inversely correlated with duodenal expression of indoleamine-pyrrole 2,3-dioxygenase-1, which is overexpressed with intestinal inflammation.[12,13] However, further studies are needed to definitively ascertain the mechanism of reduced serum tryptophan concentrations in dogs with PLE due to intestinal lymphangiectasia before any recommendations can be made regarding dietary supplementation.

Vitamins

Several studies have shown hypocobalaminemia in dogs with PLE and this has also been shown to be a negative prognostic indicator in dogs with chronic enteropathy.[1] Studies demonstrating the effects of oral cobalamin supplementation at normalizing serum vitamin B12 concentrations in dogs with chronic enteropathy have been reported.[14,15] Recommended doses for oral supplementation include 250 micrograms per day for dogs below 10 kg body weight, 1000 micrograms for dogs with body weights of 10–45 kg, and 2000 micrograms for dogs with a body weight above 45 kg. Cobalamin can also be administered subcutaneously.

Serum vitamin D concentrations are decreased in dogs with PLE and are associated with poor outcome.[4] However, a consensus regarding vitamin D supplementation in dogs with PLE with documented low concentrations has not yet been established.

Minerals and Other Micronutrients

In two separate studies, ionized calcium concentrations were decreased in all dogs with intestinal lymphangiectasia in which it was measured.[11,16] Two main mechanisms may explain this finding: first,

decreased intestinal calcium absorption may be present secondary to impaired absorption of fat and/or fat-soluble vitamin D. Second, calcium lipid precipitates may also form and contribute to hypocalcemia in these dogs. Occasionally, the hypocalcemia may be severe enough that seizures develop. Treatment in these cases should focus on intravenous calcium gluconate supplementation in the immediate term and oral vitamin D supplementation.

Some dogs with intestinal lymphangiectasia may also have hypomagnesemia, necessitating supplementation.[17] Magnesium can be orally supplemented with a dose of 1–2 mEq/kg/day with either magnesium oxide, magnesium citrate, or magnesium sulfate. Supplementation may also be required in those cases with refractory hypokalemia or hypocalcemia. The most common side effect of oral magnesium supplementation is diarrhea.

DIETARY THERAPY

The main treatment strategies for intestinal lymphangiectasia include treatment of the underlying cause if identified, reduced dietary fat intake to help decrease fat absorption and intestinal inflammation, and symptomatic treatment for gastrointestinal signs.

It is important to note that one study showed that dogs with PLE with previous lack of response to a combination of dietary therapies, glucocorticoids, and immunosuppressive medications were able to achieve remission following a dietary change.[18]

Low-Fat

Although currently there is no consensus for the definition of low-fat, veterinary nutritionists generally consider less than 20% fat on a metabolizable energy (ME) basis to be suitably low-fat. Researchers have reported increased serum albumin concentration and improvements in clinical signs after dogs with intestinal lymphangiectasia were fed a commercially available or home-prepared low-fat diet.[19] Similarly, one small retrospective study in Yorkshire Terriers with intestinal lymphangiectasia demonstrated that some dogs could respond satisfactorily in the short-term to a low-fat diet alone.[20] Also, another study showed that dietary fat restriction could be used as an effective treatment in dogs with intestinal lymphangiectasia that were unresponsive to prednisolone or experienced a relapse with dose reduction.[21]

If the gastrointestinal signs or biochemical abnormalities do not sufficiently improve with a low-fat diet, then further dietary fat reduction by feeding an ultra-low-fat diet should be pursued.

Ultra-Low-Fat

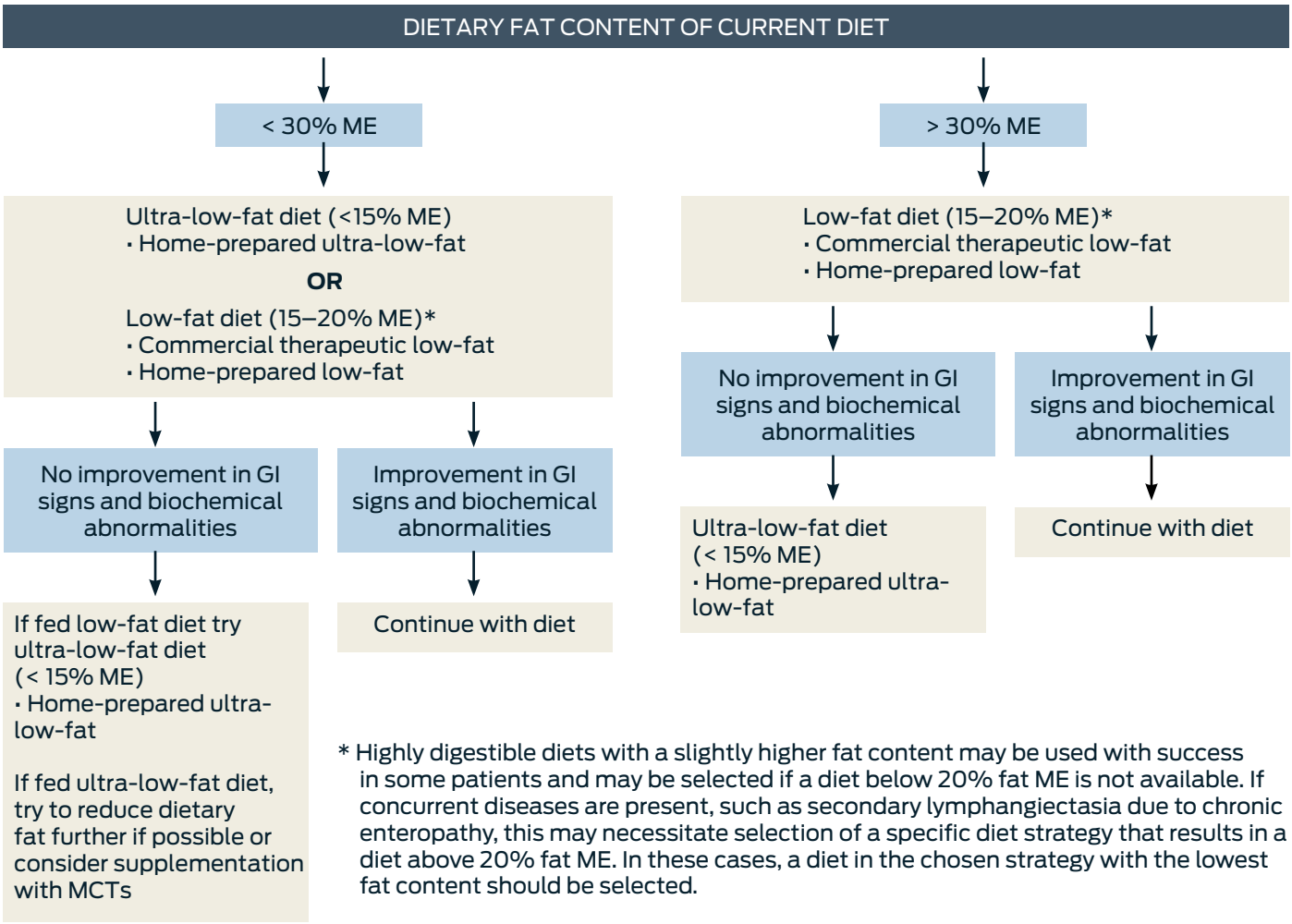
Ultra-low-fat diets are considered by the author to be generally less than 15% fat on a ME basis. Ultra-low-fat diets are not commercially available. A home-prepared diet using ingredients that are low in fat, such as cottage cheese or tilapia and white rice, would be the ideal way to achieve an ultra-low-fat diet with increased digestibility. However, consultation with a board-certified veterinary nutritionist should be sought to ensure ultra-low-fat home-prepared diets are complete and balanced and therefore still contain the minimum requirement of essential fatty acids and other nutrients.

The level of dietary fat selected will depend on the amount the dog is currently consuming. For example, between 15% and 20% fat on an ME basis (i.e., low-fat) may be chosen if the dog is currently consuming at least 30% fat (**Figure 2**). However, if the dog is already consuming less than 30% fat on an ME basis and is showing persistent gastrointestinal signs and abnormal biochemical parameters, an ultra-low-fat diet (less than 15% fat on an ME basis) can be trialled. An ultra-low-fat diet can also be chosen if the dog's clinical signs and laboratory parameters fail to respond to a commercial therapeutic or home-prepared low-fat diet in the first instance. In addition to dogs with intestinal lymphangiectasia, the author will also attempt a trial with a low-fat or ultra-low-fat diet in dogs with inflammatory PLE that are not responding adequately to dietary and/or medical management for chronic enteropathy, in case lymphangiectasia or lacteal dilation was missed on intestinal histopathology.

Fat Restriction with a Food Elimination Trial

In those dogs with inflammatory protein-losing enteropathy with secondary lymphangiectasia, a hydrolyzed or limited-ingredient novel protein diet is generally chosen due to the underlying enteropathy. However, due to the secondary lymphangiectasia, the formula with the lowest amount of fat within these categories of diets is commonly chosen. This typically results in a fat content of between 23% and 30% on a metabolizable energy basis. If the dog's clinical signs

Figure 2. Algorithm of dietary fat consideration in dogs with intestinal lymphangiectasia (ME = metabolizable energy, MCT = medium chain triglycerides)



* Highly digestible diets with a slightly higher fat content may be used with success in some patients and may be selected if a diet below 20% fat ME is not available. If concurrent diseases are present, such as secondary lymphangiectasia due to chronic enteropathy, this may necessitate selection of a specific diet strategy that results in a diet above 20% fat ME. In these cases, a diet in the chosen strategy with the lowest fat content should be selected.

and biochemical parameters do not adequately respond to the chosen diet after 2 weeks of exclusive feeding, then a therapeutic low-fat or ultra-low-fat diet can be considered. As an ultra-low-fat diet would consist of a home-cooked diet, novel ingredients can also be included to help address the underlying enteropathy. It is not uncommon for these dogs to undergo trials with different successive diets utilizing different strategies before an adequate response is seen.

DIETARY INSTRUCTIONS

Feeding smaller meals more frequently throughout the day is likely advantageous in dogs with intestinal lymphangiectasia to prevent overloading of the gastrointestinal tract. If the dog has an ideal body condition, then the number of daily calories that was previously fed can be continued. If the dog is under-conditioned, the daily number of calories should be increased by 10% increments to offset any malassimilation from the intestinal lymphangiectasia until an ideal condition is reached. One study showed that an improvement due to a change in diet in dogs with PLE is likely to be seen within 14 to 30 days.[18]

A slow transition to the new diet should take place over 7 to 10 days to help with acceptance and to assess tolerability. If a home-prepared diet is being fed, supplements such as fish oil and multivitamin/mineral blend can be added in stages to help with acceptability and assessment of tolerance.

REASSESSMENT AND MONITORING

Reassessment and monitoring are important after the new therapeutic or home-prepared diet has been initiated to ensure compliance and evaluate the effects, as well as to determine if any adjustments to the feeding plan are needed. The dog's body weight, body condition score, muscle condition score, appetite and

food intake, overall appearance and activity, as well as gastrointestinal signs should be regularly monitored. In addition, laboratory parameters such as serum albumin, globulin, and cholesterol concentrations, should be regularly assessed to determine the efficacy of the diet.

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PANCREATITIS IN CATS

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KEY TAKEAWAYS

- Feline pancreatitis is a difficult disease to diagnose and treat. The best nutritional profile for cats with this condition has not been yet established.
- Medical fasting is not recommended for feline pancreatitis given its associated risks and lack of efficacy data. Cats with pancreatitis should be fed as soon as feasible, and assisted feeding is required if voluntary intake is insufficient.
- Veterinary therapeutic gastrointestinal diets are adequate choices for cats with pancreatitis given their high digestibility and palatability, but comorbidities will affect diet choice.

DEFINITION

Pancreatitis is an inflammatory condition of the pancreas.[1] It is usually classified into acute (AP) and chronic (CP) based on histopathology, and it is generally not possible to differentiate between the two using clinical presentation.[2,3] In cats, CP is most common according to histopathology.[4]

CLINICAL SIGNS

Clinical signs and physical examination findings are non-specific, the most common being lethargy, dehydration, weight loss, and a reduction in food intake.[3,5] The disease can range from mild to severe: cats with AP might be more likely to be symptomatic whereas CP can be asymptomatic,[4] and CP might even be an incidental finding, given its high prevalence on necropsy. Cats with clinical signs can have mild, moderate, or severe disease, the latter usually requiring hospitalization.

Comorbidities, such as chronic enteropathies, cholangitis, or diabetes mellitus, are relatively frequent in cats with this disease[2,5] and more common in CP vs AP.[3] In these cases, it is difficult to identify the role, if any, that CP plays in the clinical presentation. Therefore, clinical signs associated with these comorbidities might also be present and contribute to disease severity as well as impact diet selection.

PATHOPHYSIOLOGY

Pancreatitis, especially AP, is thought to be the result of premature activation of zymogens within the acinar cells; however, there is still no clear picture on how the protective mechanisms of the pancreas to prevent this are bypassed.[6] Most feline pancreatitis cases, whether acute or chronic, therefore, are considered idiopathic, although some inciting causes have been suggested, such as certain infections, anesthesia, ischemia, trauma, and organo-phosphate poisoning.[2,6] The association of pancreatitis with inflammatory conditions of the intestine and liver (sometimes called triaditis)[6] has raised the question of a common etiology in those cases.

No associations with breed, sex, or age have been described in cats. As opposed to dogs, feline pancreatitis has not been associated with dietary indiscretion, overweight, or hyperlipidemia.

DIAGNOSTICS

Diagnosing this disease is challenging.[6] Biopsies are considered the gold standard but are very uncommon in clinical practice. In most cases, a presumptive diagnosis is based on presence of compatible clinical signs, minimum database (CBC, serum chemistry, and urinalysis), specific tests measuring pancreatic lipase (such as feline pancreatic lipase immunoreactivity, fPLI), and imaging (mainly abdominal ultrasound). While changes in CBC, serum chemistry, and urinalysis show non-specific alterations, they can be used to rule out other conditions, and to identify comorbidities and complications. Pancreatic lipase measurements are specific and sensitive, although a small proportion of

false positives are described.[7] The sensitivity is worse in mild to moderate disease compared with severe. The efficacy of abdominal ultrasound for the diagnosis of pancreatitis is considered equipment and operator dependent.

TREATMENT

Therapy[2,6,8,9] varies depending on the severity of the disease, with mild to moderate cases usually handled in an outpatient manner and more severe cases requiring hospitalization.

In hospitalized patients, treatment is supportive and includes fluid therapy, pain management, and control of vomiting and nausea (if present). Treatment will also be adjusted depending on the presence of complications (such as disseminated intravascular coagulation) and comorbidities. In outpatients with milder disease, treatment includes management of any comorbidities (**Table 1**), nausea, and analgesia. In all cases, nutritional support is a central part of management.

Key Nutrients

While there are no specific nutrient requirements described in cats with pancreatitis compared with healthy cats, and the best macronutrient profile for these patients is yet unknown, providing adequate calories and nutrients in the form of a complete and balanced, highly digestible diet is important to prevent malnutrition and its associated negative effects.[10]

Energy: While technically not a nutrient, provision of adequate energy is an essential part of the treatment in these cats. Decreased food intake is a common clinical sign before presentation which can in turn result in muscle wasting and body fat loss. Patients in a negative energy balance can have decreased organ function, alterations in the immune system, and altered intestinal barrier function.[6] Moreover, if energy intake is inadequate, cats will preferentially use important macronutrients like protein for energy rather than for other required functions.[11] Additionally, inadequate calorie intake in cats is associated with increased risk of feline hepatic lipidosis[12] (HL), especially in overweight patients.

Protein: Cats are obligate carnivores with a relatively high protein requirement.[11] Any diet fed to cats must amply meet the protein and amino acid requirements using highly digestible protein sources.

Fat: As opposed to dogs, there has been no association described between pancreatitis and food indiscretion (usually with fatty foods) or hyperlipidemia in cats. Unfortunately, there is very little research on the effect of macronutrient composition in the outcome of feline patients with pancreatitis. Moreover, there is no standard definition of what a high/moderate/low fat diet means. AAFCO[13] and FEDIAF[14] minimum for feline diets is 20% on a metabolizable energy (ME) basis, but most provide much more, ranging from 30 to 70% (or even more) ME. Canned and raw meat-based diets tend to be higher in fat than dry food. Diets that contain moderate protein or starch (such as kidney or diabetic diets) tend to be higher in fat than others. However, there is considerable overlap between different diet categories.

Therefore, fat moderation or restriction is not a common recommendation in cats. One retrospective study of cats with suspected pancreatitis[15] concluded that a diet with 45% fat (ME) was well tolerated in these cases. That said,

Table 1. Comorbidities commonly associated with pancreatitis in cats and typical dietary strategies

Disease	Typical dietary strategies
Chronic enteropathy	Highly digestible, limited ingredient, elimination diet (based on novel/uncommon ingredients or hydrolyzed protein)
Cholangitis	Highly digestible diet Protein moderation might be required if there is hepatic encephalopathy although uncommon
Diabetes mellitus	Low carbohydrate/high fat/high protein diets are commonly recommended In overweight cats, weight management is indicated

several authors have described anecdotal success with moderating fat intake, and some advise avoiding very high fat diets,[6,9] but no specific dietary fat values are proposed. Given the large overlapping in fat content of different feline diets, this author recommends assessing the fat level of the diet at diagnosis and of the available diets for this disease and, if possible, choosing a diet lower in fat for long-term management than the one being fed at presentation, especially if previous diets have not had a good outcome. It is essential to compare diets on a calorie basis and to obtain typical analysis nutrient levels from the manufacturer.

Vitamin B12 (cobalamin): Vitamin B12 is an important essential nutrient with a complex absorption process.[11] Cats with pancreatitis can have hypocobalaminemia for a variety of reasons:[16] low intake (due to inappetence), low intrinsic factor secretion (in cats, intrinsic factor is only produced by the pancreas), altered intestinal bacterial populations (dysbiosis), and decreased absorption (due to ileal disease), with the latter two more common in cats with concurrent chronic enteropathy.

Cobalamin should always be measured in cats with suspected pancreatitis and supplemented parenterally or orally[17] if found below reference ranges. Ensuring the cat is fed adequate amounts of a complete diet will also help achieve an adequate B12 provision.

Complete and balanced diet: As our knowledge on the best dietary profile and energy and nutrient needs in cats with pancreatitis is so scarce, it is important that all essential nutrients (around 40)[11,13,14] be provided in the form of adequate amounts of a complete and balanced feline diet, assuming nutrient requirements are at least equal to those of healthy cats.

COMMUNICATION TIP

The patient's nutritional assessment, especially body condition score, may impact diet selection.

Feeding Plan

A complete nutritional assessment,[18] including diet history, is important to assess risk of malnutrition and establish a tailor-made feeding plan for each patient. Factors that impact the feeding plan, among others, include body condition score, muscle condition score, and the presence of comorbidities.

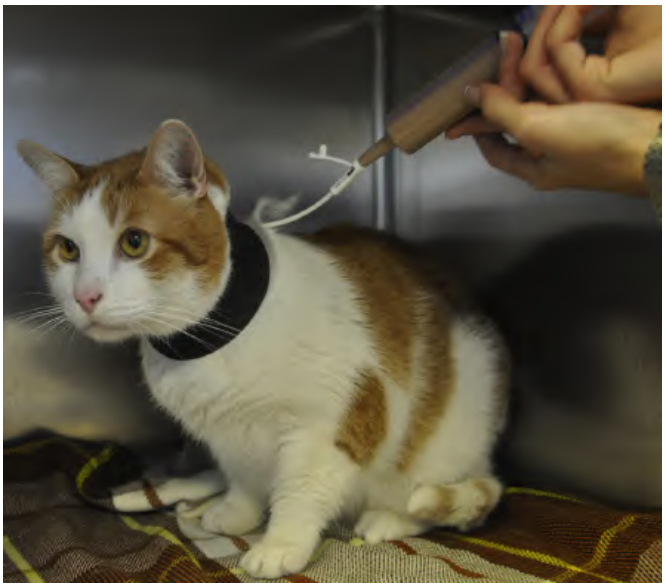
When to start: A nutritional plan should be made for a cat with pancreatitis as soon as possible. Early enteral nutrition has been shown to improve outcomes in humans with pancreatitis,[19] but data in cats is still scarce. However, delaying feeding in cats has many downsides and little benefit. Fasting these patients can worsen their nutritional status, usually already altered, and can contribute to a compromised intestinal barrier as well as increase the risk of HL. For these reasons, withholding food is not recommended and these cats should be fed as soon as it is feasible.

The ISFM has published guidelines[20] on how to manage inappetent cats in hospital, which summarizes different strategies to promote food intake as soon as possible. These strategies include the supportive treatment mentioned above (fluid therapy, pain and nausea management), constant medication review, stress reduction, addressing constipation, and establishing a feeding plan on admission.

Route: In cats with milder disease, voluntary oral feeding is the preferred option, and efforts should be made to choose a diet palatable for the individual patient. The use of appetite stimulants like mirtazapine or capromorelin (where available) can be attempted if food intake is insufficient to maintain an adequate weight and body condition,[6] although data for their use in cats with pancreatitis is still lacking.

If voluntary intake is insufficient, such as in inappetent cats or cats with severe nausea (common in more severe disease), assisted feeding is required (**Figure 1**). Enteral feeding is preferred over parenteral. Feeding tubes commonly used in feline pancreatitis are nasoesophageal, nasogastric, and esophagostomy. Short-term parenteral nutrition is only indicated if enteral feeding is not possible, and it is associated with higher mortality,[21,22] although it is possible this is due to patient selection bias. More information on critical care nutrition and feeding hospitalized patients is found elsewhere.

Figure 1. Assisted feeding of a cat with pancreatitis



Diet choice: Using a highly digestible, "low residue" (also called "intestinal") complete and balanced feline diet is a good starting point for feline pancreatitis with the current knowledge of the disease. These diets provide nutrients in an easily assimilable manner, are usually high in energy density, and tend to have good palatability. There are many options on the market to choose from. Their fat content is highly variable, ranging from 30 to 50% ME; therefore, assessing the different products available to the clinic and comparing them with the diet fed prior to presentation is important when making a final decision.

In cats with comorbidities, the specific disease(s) will also affect diet choice. For example, the use of diets based on limited uncommon ingredients or hydrolyzed protein, commonly recommended for chronic enteropathies,[23] can be used in cats with both of these diseases. These diets are also highly digestible and have variable levels of fat (ranging from 30 to 55% ME, approximately).

Other aspects to consider for diet choice include availability, cost, acceptance by the clients and patients, and route of feeding. The patient's nutritional assessment, especially body condition score, may also impact diet selection; for example, choosing a diet higher in energy density than the current diet is indicated in underweight cats.

If a feeding tube is in place, the use of critical care (convalescence) diets is common. In cats with narrow nasogastric or nasoesophageal feeding tubes, liquid convalescence diets are the best choice. Convalescence diets are canned or liquid, highly digestible, overall high in fat (>40% ME), provide ample amounts of good quality protein, and are high in energy density (≥ 1 kcal/mL). If a larger bore tube is in place, slurries made with other diets—both canned and dry—mixed with water are also an option.

Feeding amounts: The effect of pancreatitis on maintenance energy requirements (MER) is unknown and feeding amounts should be determined case by case. The diet should be fed in sufficient amounts to achieve and maintain a stable weight with an ideal body condition score (BCS). Establishing the current energy intake based on the diet history and making adjustments is ideal; for example, in an underweight cat, the energy intake can be increased by 10%. If current energy intake cannot be determined, formulas can be used to estimate MER, even though formulas have associated error and only act as a starting point. The daily allowance should be adjusted twice a month to achieve the desired weight and BCS goals. In overweight or obese patients, a weight loss plan can be implemented once the patient is stable and has a reliable appetite if weight loss is desired in these patients once they are at home. If the cat is hospitalized with a feeding tube, feeding amounts are calculated differently and the adjustments are done more frequently, reaching RER for current weight over 2–4 days.

Feeding method: For patients eating voluntarily, multiple small meals might be better tolerated.[20] Allowing underweight cats or cats with a picky appetite to graze may be indicated, but a calculated feeding plan is indicated in obese or obese-prone patients.

Follow up: The feeding plan should be adjusted according to the repeated nutritional assessment (including body weight, BCS, muscle condition, and food intake), clinical evaluation, and other diagnostics.

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PANCREATITIS IN DOGS

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KEY TAKEAWAYS

- Nutritional management of acute canine pancreatitis focuses on supportive care to control presenting clinical signs while feeding a low-fat diet.
- Dogs with acute pancreatitis with a recent history of ingestion of a high-fat meal may not need a low-fat diet long-term.
- After recovery from an acute pancreatitis episode, each patient should be monitored for signs of intolerance to the diet recommended for long-term use and feeding recommendations should be adjusted accordingly. Comorbidities should be considered in nutritional management plans and may impact dietary fat tolerance.

INTRODUCTION

Pancreatitis, or inflammation of the pancreas, is typically classified based on its presentation as either acute or chronic onset. In cases of acute pancreatitis, clinical signs are typically more severe and may require aggressive patient stabilization and hospitalization, while cases of chronic pancreatitis tend to be more difficult to diagnose due to intermittent, mild, or non-specific clinical signs. While severe acute pancreatitis episodes can cause life-threatening illness, most patients generally have an overall good prognosis for recovery and long-term management. Dietary intervention is considered a mainstay of canine pancreatitis therapy regardless of acute or chronic presentation.

PATHOPHYSIOLOGY

Stimulators of pancreatic secretion and activity in dogs include dietary protein and fatty acid intake, gastric distension, movement of low pH gastric contents into the duodenal lumen, and enteric neuropeptides.[1] Pancreatitis can develop when local safeguards are overwhelmed, resulting in early activation of trypsin and other pancreatic proteases.[2] In severe cases in which pancreatic inflammation is uncontrolled, substantial and irreversible pancreatic damage can result, ultimately placing the patient at risk of developing diabetes mellitus or exocrine pancreatic insufficiency.[3]

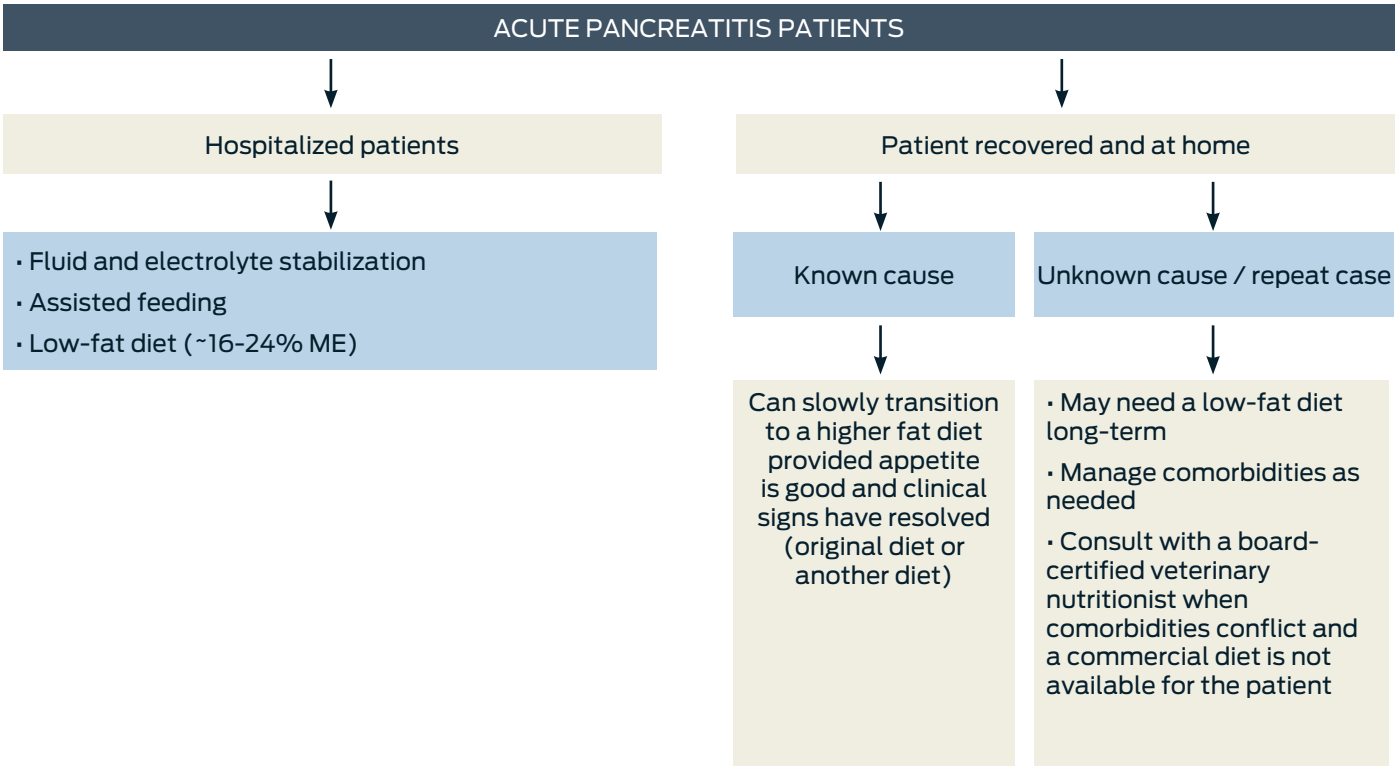
PREDISPOSING FACTORS

There are multiple well-known predisposing factors for pancreatitis in dogs. Many endocrinopathies including diabetes mellitus, hypothyroidism, and hyperadrenocorticism have been associated with pancreatitis. These endocrine diseases are often associated with obesity and hyperlipidemia, which are also risk factors for acute pancreatitis.[4] Several dog breeds are genetically predisposed to hyperlipidemia and are therefore also at an increased risk of development of pancreatitis, including Miniature Schnauzers.[5]

Drug side-effects resulting in pancreatitis are uncommon but have been associated with calcium, phenobarbital and potassium bromide, sulfonamides, clomipramine, and zinc.[4,6-10] Corticosteroids have historically been associated with pancreatitis development; however, this is an active area of research, and one study evaluated use of corticosteroids in management of acute pancreatitis episodes and demonstrated faster improvement of clinical signs.[4,11]

Critical care patients may also be at an increased risk of pancreatitis development if they experience or undergo ischemic and reperfusion injury of pancreatic tissue, abdominal trauma, or exploratory laparotomy with direct pancreatic tissue handing.[1,4] Finally, dietary indiscretion, feeding high fat table scraps, and ingestion of high protein and/or high fat containing foods also predispose dogs to pancreatitis.[4,12]

Figure 1. Management of acute canine pancreatitis episode. The algorithm shows steps for determining the route and diet selection for a dog being treated for acute pancreatitis.



DIAGNOSIS

Despite extensive research and application of diagnostic methods, there is not a pathognomonic presentation or single accurate clinical test for pancreatitis. A presumptive diagnosis of pancreatitis in the clinical setting therefore relies on multifactorial supportive evidence including patient history, clinical presentation, laboratory testing, and abdominal imaging.

A thorough diet history is key to diagnosis of pancreatitis, especially in cases with acute onset. Dietary indiscretion, commonly of high fat containing human foods, often results in gastrointestinal signs within 24 hours.[4] A complete diet history including all currently fed foods (both commercial and homemade), treats, supplements, and any foods used to administer medications should be obtained. In cases of chronic pancreatitis, a complete diet history may help correlate mild, intermittent clinical signs to specific ingredients or a high or variable dietary fat concentration.

Clinical signs are highly variable between patients for both acute and chronic pancreatitis and may include vomiting, diarrhea, hyporexia or anorexia, lethargy, abdominal pain, or pyrexia. For chronic cases, clinical signs are often more mild or intermittent. Extremely critical acute pancreatitis patients may present with profound dehydration or cardiovascular collapse and require emergency stabilization. Contrastingly, a diagnosis of chronic pancreatitis may be difficult due to mild, intermittent, or non-specific clinical signs such as difficulty maintaining muscle mass or body condition, or unintentional weight loss.

Laboratory diagnosis of both acute and chronic episodes of pancreatitis can be challenging. Elevated concentrations of serum amylase and lipase activities are of limited utility due to low specificity for pancreatitis and being highly influenced by concurrent conditions (e.g., renal disease, dehydration). Assays for canine-specific pancreatic lipase are currently available as point-of-care tests and through reference laboratories, which provide increased sensitivity and specificity for pancreatitis compared with measuring concentrations of serum amylase, lipase, or trypsin-like immunoreactivity.[4] A complete blood count, serum biochemistry panel, and urinalysis are recommended to rule out differential diagnoses. Abdominal imaging may also be performed to support a diagnosis of pancreatitis, including abdominal radiographs, ultrasound, or advanced imaging techniques. Histopathology remains the gold standard for diagnosis

of pancreatitis, although pancreatic biopsies are rarely obtained due to procedure invasiveness, cost, and risks associated with surgical or laparoscopic procedures in critical patients.

Clinically, diagnosis comes from using a combination of clinical signs, physical examination findings, abnormal pancreatic lipase enzymatic activity, and consistent findings on diagnostic imaging, and cytologic or histopathologic findings, when available. Individual tests should not be used to make a diagnosis of pancreatitis.[13,14]

INITIAL MANAGEMENT

Initial management of acute or acute-on-chronic episodes of pancreatitis focuses on patient stabilization, if indicated, followed by symptomatic care. Pain management, fluid and electrolyte replacement, anti-emetic therapy, antibiotics, and gastroprotectants may all be used depending on presentation. Nutritional support should be implemented once a patient is cardiovascularly stable. For anorexic patients, those with uncontrollable vomiting or nausea, or severely debilitated critical care patients in which oral feeding is contraindicated (such as patients receiving ventilator support or with severe neurologic impairment), parenteral nutrition should be instituted. A jejunostomy feeding tube could alternatively be considered to parenteral feeding for select cases and has been shown to be a safe and effective method to administer nutrition in severe acute pancreatitis.[15] Once clinical signs are controlled and the patient has an appropriate level of consciousness and control of their airway and gag reflex, enteral feeding should be started as soon as possible to help promote regular gastric and intestinal motility, more normalized microbiome, and enterocyte health. One recent study suggests that feeding within 48 hours of hospitalization may positively impact time to return of voluntary food intake and is associated with a lower incidence of gastrointestinal signs during hospitalization.[16] Please refer to the Practical Tool on assisted feeding and using feeding tubes for further guidance on feeding tube selection and strategies to encourage voluntary intake in a hospital setting.

KEY NUTRITIONAL FACTORS

Fat

Fat is a known stimulator of pancreatic secretion in the intestinal lumen. There is no specific recommendation for the amount of fat for dogs with pancreatitis, and some dogs may tolerate higher fat than others. An extremely general guideline would be to offer a diet that is 50% lower in fat relative to the current diet in cases of acute pancreatitis. For example, a dog that developed pancreatitis when consuming a diet containing 50% of metabolizable energy (ME) from fat may tolerate a diet with 25% of ME from fat. In that case, feeding a well-pet food marketed for an adult dog (typically ranging from 25–35% fat ME) may be appropriate for that individual. For other animals, a veterinary therapeutic diet (VTD) specifically formulated with a low-fat concentration may be indicated (approximately 16–24% fat ME or less than 2.5–3.0 g fat/100 kcal).

If a patient does not tolerate the concentration of fat in the available VTD category, an ultra-low-fat homemade diet providing 10–15% ME from fat can be formulated through consultation with a board-certified veterinary nutritionist. A homemade diet of an extremely lean protein source combined with a low-fat carbohydrate source for an extremely severe acute pancreatitis patient could be considered for short-term feeding, but it should be emphasized to the client that it is not recommended for long-term feeding if not complete and balanced.

Box 1. Possible canine pancreatitis comorbidities that may influence long-term feeding dietary fat recommendations

- Increased dietary fat
  - Chronic kidney disease
  - Low body condition
  - Reproducing dogs (gestation, lactation)
  - Growth
- Reduced dietary fat
  - Hyperlipidemia
  - Obesity/weight loss
  - Gastroesophageal reflux disease
  - Lymphangiectasia
  - Steatorrhea
  - +/- Inflammatory bowel disease/ chronic enteropathy
  - +/- Exocrine pancreatic insufficiency (EPI)

Protein

Acute pancreatitis is considered a catabolic disease process due to its inflammatory nature and can result in significant nitrogen losses.[17] The body does not maintain a protein reserve, unlike for fat or carbohydrate, and so it is important to meet a patient's daily protein requirement to prevent catabolism of lean muscle for use in acute-phase protein production and tissue repair. Dietary protein can also improve diet palatability. Because protein and free amino acids are known pancreatic stimulators, it is important to provide a moderate concentration of high-quality protein to meet needs without causing excessive pancreatic stimulation.[4] For patients with poor appetite or muscle wasting, or for patients that require long-term feeding of a low-fat diet, a higher protein diet may positively impact palatability and help maintain lean muscle mass.

Supplements

Supplementation of dietary omega-3 polyunsaturated fatty acids (PUFAs) has been shown to have a positive impact in reducing inflammation in dogs.[18] While specific amounts of omega-3 PUFAs have been recommended for multiple disease processes, including idiopathic hyperlipidemia or more general inflammatory conditions, a specific dose for canine pancreatitis has not been evaluated.[18] If omega-3 PUFAs are supplemented, the additional dietary fat content should be considered in the patient's total dietary fat intake.

The addition of antioxidants including selenium, vitamin C, vitamin E, beta-carotene, and methionine has been explored in management of human chronic pancreatitis to reduce oxidative stress.[4] Studies evaluating these individual nutrients in canine pancreatitis have not been performed.

Water

Free-choice water should always be available for pancreatitis patients to encourage normal hydration and pancreatic perfusion. In cases of intractable vomiting, hydration should be provided intravenously. Once vomiting is controlled, water may be gradually introduced.

DIETARY MANAGEMENT

Initial feeding recommendations for an acute or acute-on-chronic pancreatitis patient include feeding a complete and balanced, highly digestible, highly palatable diet. The goal is to provide a diet that does not contribute to excessive pancreatic stimulation and secretion. This means the diet should be low fat and moderate to moderately high in protein. During hospitalization, small, frequent meals should be offered to help encourage intake to meet the individual's resting energy requirement (RER) at its current body weight. Small meals may also help manage nausea, vomiting, or diarrhea, if present, and help evaluate tolerance to the newly offered food.

Once a patient is eating well and clinical signs are controlled, feeding amounts may be gradually increased, and frequency of meals decreased, to transition the pet home. Once at home, it is recommended to gradually increase feeding amounts over several days until the pet is receiving their previous calorie intake prior to hospitalization, or calculated maintenance energy requirement (MER), if their previous daily calorie intake is unknown.

For long-term management, nutritional recommendations are dependent on patient recovery, if chronic pancreatitis is suspected, if an inciting cause of acute pancreatitis was identified, or if a comorbidity has been diagnosed that requires specific dietary fat recommendations. In cases of known dietary indiscretion or ingestion of a high fat-containing meal causing acute pancreatitis, the patient should be fed a diet with lower fat than their normal diet for approximately 7–10 days, or until clinical signs have completely resolved. After this period, a patient may be gradually transitioned back to their previous commercial diet over an additional 7 to 10-day period. If at any time the dog shows evidence of regression or recurrence of pancreatitis, the diet transition should be stopped, and the low-fat diet restarted at 100% of total daily caloric requirement. Dependent on the original dietary fat concentration, a further attempt to transition to the original diet may be attempted. Alternatively, a well-pet commercial diet with a relatively lower fat concentration could be considered at this stage. Please refer to the World Small Animal Veterinary Association Global Nutrition Committee: Recommendations on Selecting Pet Foods for additional guidance on evaluating well-pet products.

For patients with chronic pancreatitis, recurrent episodes of acute pancreatitis, or those that develop acute pancreatitis with no definitive inciting cause, feeding a low-fat diet for a minimum of several weeks may be necessary. The patient may be challenged with a slightly higher fat diet after several weeks provided the patient is maintaining body weight, body condition, and muscle condition without any clinical signs of recurrence. A gradual transition over 7–10 days is recommended with any dietary change. If a patient shows evidence of intolerance, or recurrent clinical signs, a low-fat diet should be reinstituted immediately. Some patients will successfully transition to diets with moderate fat over time, while others will require feeding a low-fat or ultra-low-fat diet long-term to prevent relapse.

COMMUNICATION TIP

There is no specific recommendation for the amount of fat for dogs with pancreatitis, and some dogs may tolerate higher fat than others.

Treats should mimic feeding recommendations, and many commercially available well-pet products, nontoxic fruits, and/or vegetables would be appropriate and provide low-fat and moderate protein concentrations. These items, including added supplements, should not provide more than 10% of the daily calorie intake to prevent unbalancing the diet. In patients highly sensitive to dietary fat, even a small amount of a high-fat food or treat may be enough to trigger a recurrent episode of pancreatitis and should be avoided.

COMORBIDITIES

Comorbidities may greatly impact dietary recommendations for long-term management of pancreatitis. While several comorbidities also benefit from fat reduction, such as hyperlipidemia or lymphangiectasia, other disease processes may have an indication to provide a higher fat content to increase palatability and diet energy density. Alternatively, a commercially available product may not meet the multiple nutritional needs of the patient, such as incorporation of limited ingredient, novel ingredient, or hydrolyzed protein feeding strategies for management of adverse food response. Diets formulated for other conditions with lower fat concentrations may be suitable for long-term feeding but may not be tolerated in patients with severe acute pancreatitis. Please refer to Nutritional Management of Patients with Multiple Conditions for further discussion.

REASSESSMENT AND MONITORING

Body weight, body condition scoring, and muscle condition scoring should be performed at all recheck evaluations. A thorough diet history should be obtained at each veterinary visit to ensure that feeding strategies are being followed. This is particularly important in patients with recurrent clinical signs. Additional parameters to recheck in pancreatitis patients include hydration status, appetite consistency, subjective comfort during abdominal palpation, and history of recurrence of gastrointestinal signs. Frequency of rechecks should be based on case severity. Acute pancreatitis patients may be rechecked 1–2 days after hospital discharge to ensure they are eating consistently and maintaining weight and hydration, while chronic pancreatitis patients may be rechecked every 2–4 weeks, or at longer intervals if doing well at home. If a patient shows clinical signs or physical exam changes suggesting they are not tolerating the current feeding strategies, including recurrent gastrointestinal signs, weight loss, muscle condition loss, or poor hair coat, a full patient assessment, diagnostic testing, and a diet assessment should be performed.

Studies investigating the use of serial imaging for monitoring chronic pancreatitis or adjusting nutritional targets have not been performed. However, repeat imaging may be useful for ruling out differential diagnoses, particularly in patients that present with recurrent or new clinical signs.

CONCLUSION

Feeding a low-fat diet is recommended for the initial recovery period of acute canine pancreatitis. Patients with an identified inciting cause, such as ingestion of a high-fat meal, may not require a low-fat diet for long-term feeding and may tolerate a gradual transition to a

diet with moderate fat. Dogs with a history of chronic pancreatitis, repeat episodes of acute pancreatitis, or comorbidities, or those with clinical signs indicating they are not tolerating their current dietary fat concentration, may benefit from a lower fat diet long-term. After initial diagnosis and recovery from an acute pancreatitis episode, regular rechecks are critical for identifying patients with mild signs of ongoing disease and to allow for dietary and supportive care adjustments as needed. For patients with comorbidities, or those that have specific dietary requirements not met by a commercially available product, consultation with a board-certified veterinary nutritionist is recommended.

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CONSTIPATION IN CATS

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KEY TAKEAWAYS

- There is a need for well-designed scientific studies to further investigate the role of nutrition in the management of cats with constipation.
- Dietary treatment of cats with constipation consists of increasing water intake; a moderate content of dietary fiber; and weight loss if the cat is overweight.
- Megacolon requires a different nutritional intervention compared with less severe feline constipation.

INTRODUCTION

Definitions

Feline constipation is defined by a reduced defecation frequency and/or difficulty in passing feces. *Obstipation*, on the other hand, refers to a loss of function of the ability to defecate normally.[1] *Megacolon* is characterized by impaired intestinal tone and loss of colon structure and function.[2] Most cases of feline megacolon are idiopathic, while a smaller proportion is due to pelvic narrowing, for example, after conservative treatment of pelvic fractures.[3] 'Dilated' megacolon is considered the end stage of idiopathic megacolon with permanent loss of colon structure and function, and often requires colectomy. On the other hand, "hypertrophic" megacolon due to obstructive lesions may be reversible with early pelvic osteotomy.[1] Due to its nature, megacolon requires a different dietary treatment plan compared with less severe constipation and obstipation.[4] Since recurrent episodes of constipation can eventually lead to megacolon,[1] managing chronic constipation and preventing future episodes as best as possible are very important.

Risk Factors

Multiple medical conditions such as disease-associated dehydration, pelvic fractures, neuropathies, sacral spinal cord disease, overweight body condition, and primary or secondary megacolon have all been previously mentioned as risk factors for chronic constipation in felines.[5,6] In the author's experience, degenerative joint diseases and endocrinopathies can also be associated with constipation. Also, hospitalized cats may be at risk of developing constipation, as they may be reluctant to use a different type of litter and/or litter box.[7] However, not all these associations have necessarily been supported by scientific studies. Interestingly, a recent study comparing a cohort of 189 cats with constipation/obstipation with a control group of 99 cats on an emergency service identified increasing age, being overweight, being diagnosed with chronic kidney disease (CKD), and having a previous episode of constipation as risk factors for constipation.[6] Water imbalance, electrolyte disorders (such as hypokalemia, which alters smooth muscle motility), and pharmacological treatment (such as the use of aluminum phosphate binders) may all contribute to the higher risk of constipation in feline CKD.[8] A recent study also showed that defecation frequency was significantly lower in CKD cats compared with healthy cats.[9] Greater individual variability of total GI transit in older versus young cats[10] may explain why older cats are more prone to constipation. Since a previous episode of constipation predisposes cats to future episodes,[6] successful long-term prevention is very important.

DIETARY TREATMENT AND PREVENTION

Treatment of feline constipation depends on the severity of the constipation and the underlying cause. No medical treatment may be required in the case of a very mild first episode of constipation, while surgery such as a subtotal colectomy may be required in idiopathic megacolon.[1] Treatment of more severe

cases is multimodal and consists of a combination of eliminating the cause, if possible, as well as dietary and medical treatment (**Table 1**). Risk factors should be addressed for successful long-term prevention of future episodes of constipation where possible, and these include diet (intake of indigestible materials), environmental conditions (hospitalization, change in routine and activity), dehydration and electrolyte imbalances (e.g., CKD), iatrogenic (drug therapy), colon obstruction, and neuromuscular disease (spinal cord disease, megacolon).[11]

Diet is mentioned as an important factor in preventing constipation, but the number of studies investigating the effect of dietary treatments in cats with constipation is very limited. Clinically, successful dietary treatment has consisted of 3 main factors: increasing water intake, adjusting fiber intake, and tackling obesity, if present.

Increasing Water Intake

To the author's knowledge, there are no specific studies investigating the effect of increasing water intake in constipated cats, but some measures to enhance water intake in cats with feline lower urinary tract disorders may also be relevant to constipated cats from basic pathophysiological reasoning (**Box 1**). In CKD cats this may be even more important, as dehydration is probably one of the important pathways involved in constipation of this particular group.[8] In this regard, it may be beneficial to switch to a wet diet or add water to a dry diet.[12] Although feeding a dry diet alone was not found to be a risk factor for feline constipation in one study,[6] it may still be a valuable and simple approach, as the total volume of water ingested (from drinking water and food) was significantly higher in cats fed wet diets[13] and this would help to address dehydration as a contributory factor in constipation.

Preference for a particular water source and/or adding flavors to the drinking water can also be investigated by motivated owners. Zanghi et al showed an increased preference and an increased voluntary water intake with a nutrient-enriched water source compared with tap water. The addition of a poultry flavor to the nutrient-enriched water significantly increased water intake compared to the nutrient-enriched water without flavoring.[14,15] And although providing running water by using fountains or special water bowls may not be as successful for improving hydration as originally thought,[16,17] they may be useful in individuals because some cats do have clear preferences.[17]

Interestingly, a recent study found cats' unique tongue anatomy allowed them to lift more water per lap when the viscosity of the water was increased. Indeed, water intake was significantly increased by 21–25% by adding 1% methylcellulose to drinking water.[18]

Table 1. Different aspects of prevention and multifactorial treatment of feline constipation

Eliminate cause/decrease risk factors for feline constipation[4,5,6,7,11]	Dietary prevention/treatment[8,11,12,20,25]
Diet: prevent intake of indigestible materials	Stimulate water intake
Environment: avoid change in routine & activity; create environment during hospitalization as similar to home situation (e.g., litter and litterbox)	Choose a diet with moderate amount of mixed type of fiber or supplement fiber to a lower fiber maintenance or veterinary therapeutic diet
Avoid and treat dehydration and electrolyte imbalances (e.g., in cats with CKD)	Supplement with a probiotic
Avoid drugs that decrease intestinal motility	
Treat disease that may increase the risk of constipation: pelvic fracture, neuromuscular disease (e.g., spinal cord disease), obesity	

Of course, drinking water must be fresh and water bowls must be cleaned regularly, unless individual preference tests show otherwise.[19]

Dietary Fiber

Moderate amounts of fiber are often recommended in the treatment of feline constipation.[20] There are 2 main types of dietary fiber: insoluble and soluble.[21] Insoluble fibers such as cellulose are poorly or non-fermentable and can improve motility by a stretch response. They are therefore called *bulk-forming laxatives*.[1,21] Soluble fibers such as pectin, guar gum, and psyllium are fermented by the GI microbiota and increase short-chain fatty acid (SCFA) concentration,[21] which has been shown to have a prokinetic effect on the smooth muscles of the large intestine of cats in vitro.[22] It is also known that oversupplementing soluble fiber induces soft stools due to the osmotic effect of high SCFA production.[23] In healthy cats, high doses of oligofructose or inulin significantly increased the number, volume and moisture content of stools, and also increased fecal SCFA concentration.[24] Some soluble fibers such as psyllium are also viscous and have water binding capacities.[23] Highly fermentable polysaccharides such as lactulose are sometimes also called *hyperosmotic laxatives*.[1]

Box 1. Strategies to increase water intake in cats with constipation

- Provide fresh, clean water at all times
- Clean water bowls daily
- Offer a variety of water bowls and water sources
- Feed canned food or make dry food wet
- Use water fountains or address other individual preferences for drinking
- Add flavoring to water
- Use hydration supplements (e.g., nutrient-enhanced or viscous water-based products) to increase water intake

While there may be many benefits from increasing dietary fiber in feline constipation from a pathophysiological understanding, to the author's knowledge, there are only two uncontrolled studies investigating the effect of dietary fiber in feline constipation. Freiche et al.[11] showed clinical improvement in 2 field trials in 93 and 82% of cases (n: 15 and 51, respectively) from a commercially available moderate fiber diet. Fecal consistency improved significantly and fewer cats needed medical treatment (cisapride and lactulose). The commercial diet used in the study contained 0.7–0.75 g of crude fiber and 2.91–2.98 g of total dietary fiber per 100 kcal. Psyllium hulls and seeds were the first added fiber source in the ingredient list, but the diets also included chicory pulp, fructooligosaccharides, and a source of mannanoligosaccharides. The clinical response did not differ between idiopathic versus other causes of constipation.[11] These promising results should be confirmed in a randomized placebo-controlled trial with diets that differ only in fiber content and composition.

A second preliminary study concerned the clinical effect of a probiotic in feline constipation.[25] A small uncontrolled study showed positive results in 7 chronically constipated cats and 3 cats with idiopathic megacolon by adding a probiotic to their diet. The multistrain probiotic (8 strains of lactic acid bacteria) significantly improved stool consistency, feline chronic enteropathy activity index and some morphological parameters after 90 days of treatment.[25] Again, these promising but preliminary results need to be further investigated before routinely recommending probiotics in constipated cats.

PRACTICAL DIETARY ADVICE

Diet

In anticipation of future well-designed studies, a commercially available diet, preferably a wet diet, with moderate amounts of mixed fiber is preferred in constipated cats without megacolon, as these diets are complete and balanced. If water intake is low, or if a dry diet is fed, enhancing water intake could be helpful. However, supplementing fiber to an individual diet can also be done in cases with specific nutritional needs due to other diseases. A typical example where fiber supplementation may be necessary is constipated CKD cats where a kidney diet is recommended.[8] For example, some early-stage kidney diets contain extra fiber, but these diets may not be suitable for more advanced stages of CKD that can then benefit from fiber supplementation on top of a traditional renal therapeutic diet. Another benefit of supplementing fiber to a maintenance or veterinary therapeutic diet is the fact that it can be tailored to individual needs.

Lactulose (0.5 mL/kg BW every 8–12 hours with tapering to effect) is often used in this way.[1] Adding pumpkin is a commonly used tactic for constipated cats to add both water and fiber to a cat's diet. Canned pumpkin contains low amounts of fiber on an as fed basis but is very high in moisture. If the cat finds the pumpkin palatable, supplementation with pumpkin can increase both fiber and water intake. Psyllium, which is soluble fiber, is another option to supplement a lower fiber canned or dry diet and can be supplemented at up to 1–4 tsp or 5–20 grams per day of a pure psyllium supplement.[8]

To avoid impaction of fiber in the colon, optimal hydration before introducing a moderate fiber diet is very important, especially in cases where insoluble fiber is increased[1] as this can lead to larger and drier fecal mass.[21]

Weight Loss

Since being overweight was found to be a risk factor for constipation,[6] a weight loss plan may be an important additional factor for successful long-term prevention of feline constipation. Obesity was considered an independent risk factor associated with feline constipation because it can make the posture to defecate more difficult due to exacerbation of orthopedic or neurological disease.[6] In those cases, a classic weight loss program using a high-fiber, low-calorie diet can be started as long as the acute phase of constipation is adequately treated medically and provided the owners ensure adequate water intake. Although there is no scientific evidence, it is possible that diets with high concentrations of insoluble fiber may lead to greater and drier fecal mass.[21] Wet weight loss diets may be preferred in many cases because of their higher water content.

Megacolon

Because the structure and function of the colon are abnormal in megacolon, additional insoluble fiber is generally contraindicated[21] although fiber supplementation may be effective in some early cases of megacolon, where the colon still has some ability to contract.[4] In the majority of cases, a highly digestible low-fiber diet is preferred.[26] If appetite is decreased, the author prefers a recovery or convalescence diet, because those diets are easily digestible, high in energy and other nutrients, highly palatable, and low in fiber. Lactulose can also be used and custom-dosed in addition to such a diet.

COMMUNICATION TIP

"Clinically, successful dietary treatment has consisted of 3 main factors: increasing water intake, adjusting fiber intake, and tackling obesity, if present."

Colectomy may be needed in some cases of megacolon, but this may result in mild to moderate diarrhea for several weeks after surgery.[1] Due to compensatory changes in the small intestine, such as increased villus height, increased enterocyte height and density, stools are generally soft and become more formed about 3 months after subtotal colectomy, but the fecal frequency generally remains slightly increased.[3]

CONCLUSION

Individualized dietary treatment is an important factor in successful treatment of feline constipation. Factors that may impact management include fiber, water, and food form, in addition to medical, environmental, and surgical management.

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ESOPHAGEAL DISORDERS AND DYSPHAGIA IN DOGS

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KEY TAKEAWAYS

- The anatomical categorization of the animal's swallowing impairment into oropharyngeal and/or esophageal causes followed by determination of the pathophysiologic process (structural versus impaired motility) is pivotal for optimizing medical and dietary therapy.
- Utilization of swallowing fluoroscopy is highly valuable for optimizing the selection of different foods and food consistencies for dysphagic patients and monitoring response to therapy.
- Increasing bolus viscosity from liquid to pudding consistency significantly reduces the prevalence of aspiration in patients with oropharyngeal dysphagia.
- There is no specific consistency of ingesta that has been shown to be most reliable for facilitating the transit of esophageal contents into the stomach of dogs with megaesophagus.

INTRODUCTION

Deglutition is the process of swallowing and is a complex mechanism that involves a highly coordinated activity of 31 pairs of striated muscles and 5 cranial nerves with nuclei in the brainstem functioning to clear food and drink from the oral cavity and pharynx into the esophagus and stomach at an appropriate rate. Any disruption in the swallowing mechanism can result in dysphagia with consequent aspiration, pneumonia, malnutrition, dehydration, and an overall reduced quality of life.[1-4]

The exact prevalence of swallowing impairment in dogs is unknown, but at the University of California, Davis, nearly 1% of 105,000 dogs presenting to the Small Animal Clinic over a 10-year period between 2003 and 2013 were evaluated for a swallowing abnormality. The prevalence of dysphagia is far more common in people, in which 1 of 6 adults reported experiencing difficulty swallowing,[5] and the risk of dysphagia is even higher in older people.[6] Sarcopenia is a syndrome characterized by the loss of lean body mass and strength in the absence of disease, and is an important cause of decreased glossal volume and glossal strength in geriatric human patients, contributing to impaired propulsion of the bolus and oropharyngeal dysphagia.[7,8] Sarcopenia and cachexia are also important syndromes in geriatric animals,[9] although the role of these syndromes in oropharyngeal function and esophageal motility has not been elucidated in dogs to date.

ANATOMICAL CATEGORIZATION OF DYSPHAGIA

The anatomical categorization of dysphagia into oropharyngeal and/or esophageal causes followed by determination of the pathophysiologic process (structural versus impaired motility) is pivotal for optimizing medical and dietary management.[10,11] A thorough clinical and dietary history and a physical examination are pivotal in helping to distinguish the anatomic location and likely cause of the swallowing impairment. Diagnostic testing including survey thoracic and cervical radiographs, swallowing fluoroscopy, and/or esophagoscopy typically provides the clinician with the information needed to localize the dysphagia and determine the underlying cause.

DIAGNOSTIC STRATEGY FOR ASSESSING DYSPHAGIA

Determination of the Clinical and Dietary History

Determination of the animal's dietary history as well as its body condition score (BCS) and muscle condition score (MCS) should be routinely performed in all dysphagic animals. Dysphagia questionnaires such as the Eating Assessment Tool (EAT-10)[12] are commonly used in people to assess the severity of dysphagia,

measure quality of life, and monitor treatment response. A Dog Swallowing Assessment Tool (Dog-SAT) is a similar questionnaire currently being validated by the author to assess the severity of swallowing impairment, determine the anatomic localization of disease, and monitor treatment response. The Dog-SAT questionnaire investigates the timing of the dog's swallowing impairment in association with meals, and helps determine the type of food consistency that the animal has difficulty swallowing. A limitation of the survey is that it relies heavily on the recognition of pet owners to accurately gauge the signs of swallowing impairment in their pets.

In the absence of a validated questionnaire for dogs, there are important questions that veterinarians should ask when obtaining the history from the owner of a dysphagic dog. Examples of questions that involve feeding or management practice and that can help prioritize the differential diagnosis list are highlighted in **Box 1**.

A dietitian is an indispensable part of the dysphagia multidisciplinary team in human medicine, and evaluates the nutritional risk of the patient and the presence of malnutrition and sarcopenia. In addition, the dietitian performs a nutritional assessment on the dysphagic patient and evaluates the patient's ability to swallow different textures and viscosities of food with a speech swallow therapist. This highlights the importance of the role of nutrition in management of small animals that are dysphagic as well.

Box 1. Questions veterinarians should ask when obtaining a history from the owner of a dysphagic dog

1. **What is the temporal pattern of the dog's swallowing impairment?**
   Dogs with oropharyngeal dysphagia typically exhibit signs within seconds of food or water consumption. In contrast, dogs with esophageal dysphagia usually exhibit signs seconds to hours following food or water consumption.
2. **What is the association of dysphagia with meals?**
   Gastric distension following a meal can exacerbate hiatal herniation and gastroesophageal reflux (GER). It is important to distinguish dogs with true dysphagia from dogs that regurgitate after rapidly ingesting their meals. The latter problem can be solved much more easily with use of a dog bowl that slows food intake.
3. **What is the dog's tolerance to eating kibble versus canned food, and drinking water?**
   Dogs with cricopharyngeus muscle dysfunction (CPMD) typically experience exacerbation of dysphagia when drinking water, whereas animals with an esophageal structural disorder (stricture, mass) tolerate water and show exacerbation of signs when ingesting canned food or kibble consistency in particular.
4. **What is the dog's BCS?**
   Hiatal herniation and GER are exacerbated in obese patients.
5. **What is the dog's recent medication history?**
   Administration of clindamycin, doxycycline, tetracycline, or non-steroidal anti-inflammatory drugs (NSAIDs) can induce esophagitis or esophageal stricture formation.
6. **What is the fat content of the dog's diet?**
   High-fat diets in dogs can delay gastric emptying and predispose to GER with consequent esophagitis.
7. **Has there been a recent change in the diet that was associated with exacerbation of the dysphagia?**
   Dietary proteins can be associated with food-responsive gastropathy and consequent delayed gastric emptying or can be associated with eosinophilic esophagitis.

Observation of the Dysphagic Animal Eating and Drinking

The importance of carefully observing the dysphagic dog while eating (kibble and canned food) and drinking is pivotal for determining its ability to meet its caloric and water requirements, and to determine its ability to swallow food and water with no respiratory complications (**Figure 1**). Observing the patient eating and drinking also helps localize the problem to the oropharynx or esophagus. This study can be easily accomplished by observing smartphone video recordings captured by the pet owner or alternatively performing a feeding trial in the hospital setting. Dogs with an abnormal oral phase of swallowing typically have difficulty with prehension or aboral transport of a bolus to the tongue base, underscoring the importance of performing a comprehensive oral examination. Oropharyngeal swallowing impairment affecting the pharyngeal phase of swallowing is often associated with non-specific signs including gagging, retching, coughing, food falling from the mouth, and multiple swallowing attempts before a bolus is moved successfully into the proximal esophagus. Cricopharyngeus muscle dysfunction, with signs similar to those seen with pharyngeal disorders, causes abnormal bolus transport through the upper esophageal sphincter (UES). Dogs with esophageal strictures or esophagitis typically exhibit evidence of regurgitation or odynophagia seconds to minutes following bolus swallowing, whereas dogs with megaesophagus (ME) can exhibit evidence of regurgitation hours following ingestion of a meal.

COMMUNICATION TIP

"Any disruption in the swallowing mechanism can result in dysphagia with consequent aspiration, pneumonia, malnutrition, dehydration, and an overall reduced quality of life."

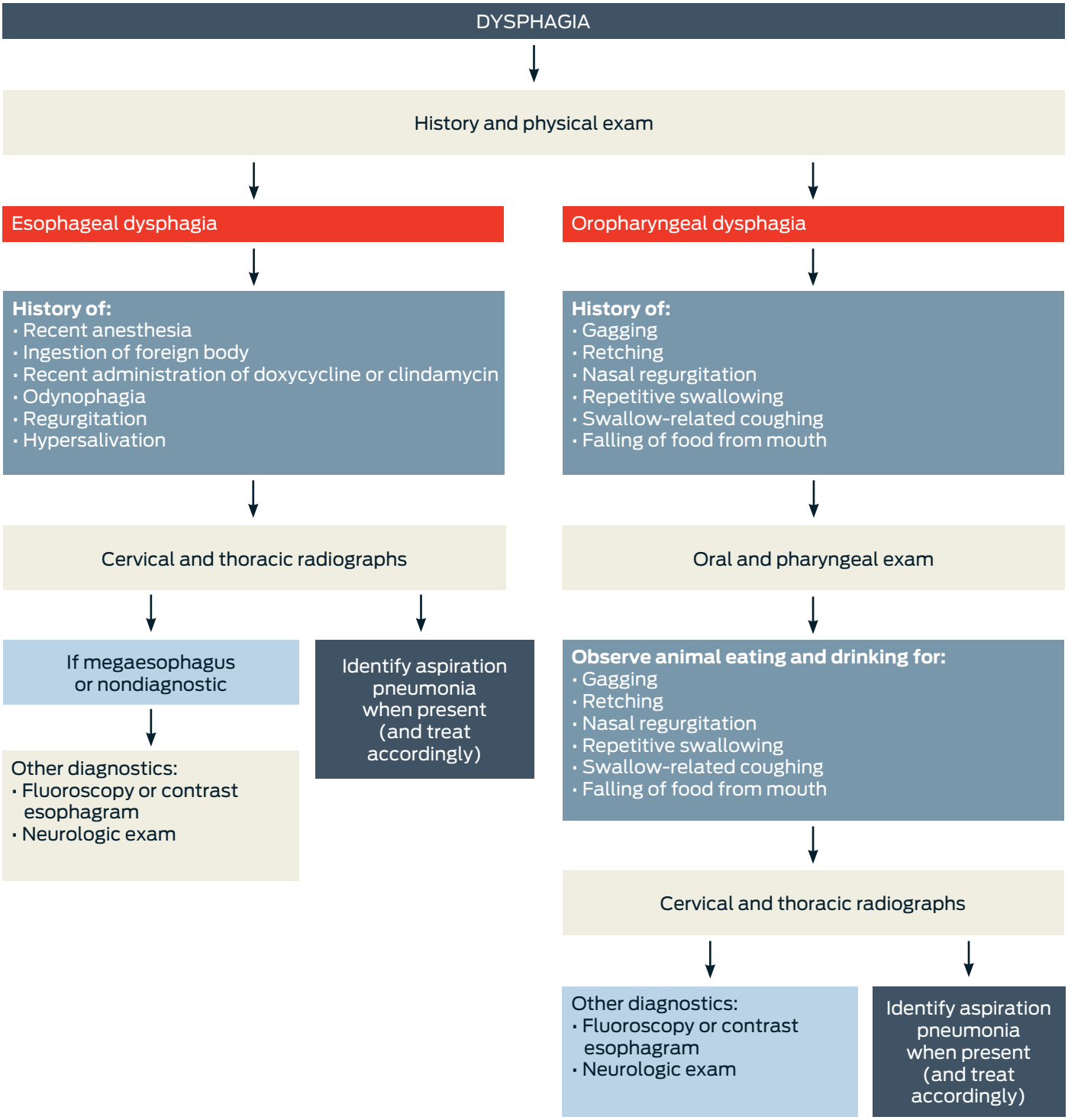
Further Diagnostics

Food bolus rheology is the study of flow and deformation of the food bolus. The rheological properties of foods entering into the mouth are fundamentally a function of the food composition, and are assessed in dysphagic human patients by performing a volume-viscosity swallowing test (V-VST). This test is particularly helpful in people with oropharyngeal dysphagia[13] and starts with low-volume (5-mL) bolus feedings of nectar (thick viscosity) with incrementally increasing volumes, followed by lower viscosity liquids of increasing volume (up to 20-mL) if the patient successfully passes the nectar trial. In contrast, if the patient exhibits impairment of efficacy or safety of swallowing while trialing nectar of thicker viscosity, the patient will immediately be tested with pudding trials according to graduated volumes, thus circumventing liquid viscosity altogether.

The V-VST has been shown to be a safe, quick and accurate clinical method, with sensitivity and specificity for impaired swallowing safety (laryngeal penetration or aspiration) of 87% and 81%, respectively.[13] The V-VST is helpful to determine the volume and viscosity of liquid the patient requires for safe and effective swallowing. Ongoing use of the V-VST serves as a tool for monitoring patient progress over time, suggesting the need to adjust volume and viscosity recommendations and/or to order further tests such as swallowing fluoroscopy. Increasing bolus viscosity from liquid to pudding significantly reduces the prevalence of laryngeal penetration and aspiration in 98.9% of patients with oropharyngeal dysphagia.[13,14] In addition, solid foods that require chewing may prove challenging for people with dental issues or weakness of the masticatory muscles, necessitating the dicing, chopping, mincing, or pureeing of the food to optimize deglutition.[15] This information can be applied to dogs but unfortunately, there is a dearth of research assessing food texture properties. In dogs, observation of the animal eating is essential because we lack information about the ideal adhesiveness, cohesiveness, firmness, and viscosity of food in dysphagic dogs, and there is a lack of universally standardized guidelines to describe the most appropriate modification of foods.

In dysphagic canine patients lacking a recognized structural cause of their dysphagia based upon physical examination of the oral cavity (e.g., glossal tumor, glossal weakness, oropharyngeal foreign body)

Figure 1. Algorithm to aid in diagnosis and determining the underlying cause of dysphagia



and survey radiographs of the neck and thorax (e.g., esophageal foreign body, vascular ring anomaly), implementation of a contrast static esophagram or swallowing fluoroscopy study can be extremely helpful to further identify the cause of the dysphagia and assess response to the feeding of different food consistencies. A contrast static esophagram is performed by obtaining baseline survey radiographs (ideally 3 views) and then administering 15–30 mL of 60% weight/volume barium sulfate suspension via syringe into the lip fold. Radiographs of the thorax are immediately repeated following swallowing of the bolus to assess oropharyngeal function or esophageal transit time. Different consistencies of barium (e.g., paste, barium mixed with canned food, or barium mixed with kibble) can be administered to determine esophageal transit time and abnormal retention of the contrast bolus. While swallowing fluoroscopy is not readily available at all veterinary hospitals, the main advantage of this diagnostic modality over a contrast esophagram is that the procedure is dynamic and allows veterinarians to determine the timing, coordination, and extent of opening and closing of the upper and lower esophageal sphincters, and is superior for assessing primary and secondary peristaltic contractions and their coordination. Gastroesophageal reflux and hiatal herniation can also be observed more comprehensively with swallowing fluoroscopy studies. In addition, the feeding of liquid barium, barium-soaked canned food, and barium-soaked kibble via swallowing fluoroscopy is superior for optimizing the selection of foods with different consistencies for dysphagic canine patients.[16-18]

MANAGEMENT OF COMMON CANINE ESOPHAGEAL DISORDERS

Cricopharyngeus Muscle Dysfunction

Cricopharyngeus muscle dysfunction (CPMD) is a congenital or acquired neuromuscular disorder characterized by failure of the UES to relax (achalasia) or a lack of coordination between UES relaxation and pharyngeal contraction (asynchrony). Affected dogs have abnormal transport of the bolus from the hypopharynx to the proximal esophagus and demonstrate progressive swallowing impairment (typically worse when drinking water) before weaning. Clinical signs are characterized by repeated attempts to swallow, gagging, retching, nasal regurgitation, and coughing.

Definitive treatment for CPMD involves surgical myotomy or myectomy of the cricopharyngeus muscle.[19] Less invasive procedures for the temporary resolution of the disorder involve injection of botulinum toxin into the cricopharyngeus muscle[20] or serial double-balloon dilations of the UES.[21]

Nutritional management is focused on altering the viscosity of water by adding cornstarch-based formulas to create a mildly thick (nectar) or moderately thick (honey) consistency. In addition, flavored ice cubes with beef or chicken broth can be used to facilitate water intake to optimize hydration status. Melons with high moisture content (watermelon and cantaloupe have some of the highest moisture contents of fruits, > 90%) can be used to augment water intake in affected dogs. Affected dogs tolerate the slow feeding of diminutive boluses of kibble (4–5 pieces of kibble per mouthful every 30 seconds) reasonably well. Enteral feeding via a gastrostomy tube (surgical gastrostomy or percutaneous endoscopic gastrostomy [PEG] tube) is a viable alternative in dogs that are unable to undergo surgical or medical management of their CPMD; however, aspiration of saliva with subsequent pneumonia can occur despite the use of enteral feeding devices.

Esophagitis

Esophagitis is an acute or chronic inflammatory disorder of the esophageal mucosa that occasionally involves the underlying submucosa and muscularis. It may result from a variety of causes including ingestion of caustic agents, chronic vomiting, medications such as doxycycline and clindamycin, esophageal foreign bodies, and GER associated with general anesthesia or hiatal hernia. Animals with mild inflammation may exhibit no clinical signs, whereas animals with moderate to severe esophagitis may exhibit signs of anorexia, swallowing impairment, odynophagia, regurgitation, and hypersalivation. Coughing may be observed with concurrent aspiration pneumonia.

Mild esophagitis usually resolves with minimal treatment other than feeding smaller volumes of fat-restricted canned or soaked kibble meals more frequently to enhance gastric emptying and minimize GER. Animals with moderate to severe esophagitis should be managed with gastric acid suppressants (proton pump inhibitors), diffusion-barriers (sucralfate), prokinetics (cisapride or metoclopramide),

and both topical (viscous lidocaine gel) and systemic analgesics. Gastrostomy tube feeding is infrequently needed but may be indicated for the management of patients with severe, intractable esophagitis.

Megaesophagus

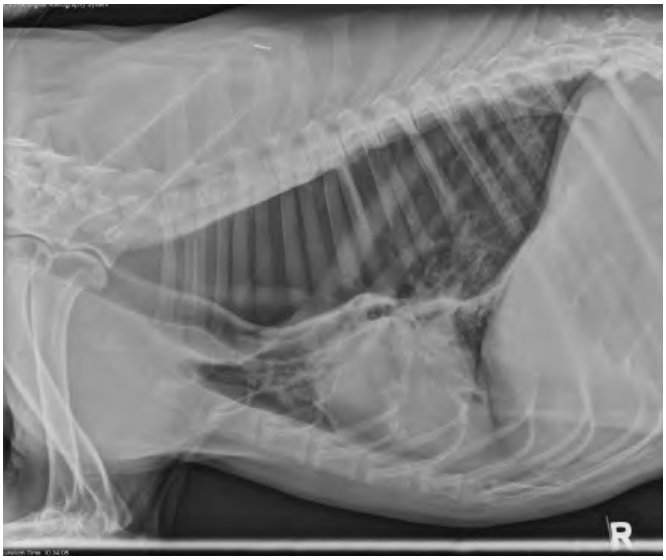
Megaesophagus (ME), the most common cause of regurgitation in dogs, is characterized by focal or diffuse esophageal dilation and concurrent esophageal dysmotility (**Figure 2**). The disorder can be congenital or acquired; however, the acquired form is more common and can be idiopathic or secondary to a recognized disease. Approximately 60% of dogs with ME have esophageal achalasia, a primary esophageal motility disorder characterized by lack of esophageal peristalsis and by partial or absent relaxation of the lower esophageal sphincter (LES) in response to swallowing.[16,22] Consequently, there is a functional obstruction at the level of the gastroesophageal junction which causes impairment of esophageal emptying.

Affected animals may suffer from malnutrition and aspiration pneumonia due to the frequent episodes of regurgitation (**Figure 3**). An underlying cause for ME should always be sought to optimize treatment and outcome. Treatment of acquired idiopathic ME associated with esophageal achalasia can involve pharmacological (sildenafil),[23] pneumatic dilation,[24] or surgical strategies (Heller myotomy and fundoplication)[25] to treat the hypertonic LES. Direct injection of botulinum toxin into the LES of patients with esophageal achalasia has also shown moderate effectiveness in people and in dogs.[22,26]

Dogs with ME can benefit from feeding practices designed to maximize food delivery to the stomach while minimizing the risk of aspiration. The application of gravity-assisted feeding whereby the dog is fed in an elevated position with the cranial aspect of the animal elevated or in a specialized feeding chair (Bailey chair) is pivotal for facilitating bolus transit from the hypopharynx to the LES (**Figure 4**). Dogs should remain elevated and/or in the Bailey chair for approximately 20–30 minutes after finishing a meal, depending on food viscosity and severity of esophageal impairment and esophageal achalasia. The duration of elevated positioning following a meal can also be determined via results of a contrast esophagram or swallowing fluoroscopy study (see below). There is no specific consistency of ingesta that has been shown to be most reliable for facilitating the transit of esophageal contents into the stomach of dogs with ME, and two studies in dogs with ME confirmed the need to alter the initially recommended food consistency in 50% and 29% of the dogs, respectively, based on fluoroscopic swallowing assessment.[17,18] Fluoroscopic swallowing

Figure 2. A 3-year-old male neutered French Bulldog with a sliding hiatal hernia and consequent esophagitis undergoing a feeding trial to evaluate the dog's swallowing function. He is being offered water and small boluses of canned food and kibble.

Figure 3. A 5-year-old female spayed German Shepherd dog with acquired idiopathic megaesophagus. The esophagus is diffusely and severely gas distended and drapes over the cranial thoracic trachea, causing ventral deviation of the trachea and marked widening of the mediastinum. Patchy alveolar opacity is present in the ventral aspect of the left cranial lung lobes.



assessment in affected dogs allows the clinician to determine which food consistency (liquid, canned meatballs, slurry [milkshake consistency], or kibble) most reliably facilitates bolus transit and LES relaxation in affected dogs. A contrast static esophagram can also be performed to help optimize selection of food consistency for dogs with ME and possible esophageal achalasia. The dog should be fed a barium slurry in an upright position (Bailey chair), and thoracic radiographs should be obtained after the dog has been maintained in an upright position for 15 minutes. The barium slurry is followed by barium mixed with canned meatballs if the dog has successfully emptied the barium slurry into the stomach. The dog should ideally be maintained in an upright position following the feeding of different food consistencies. The canned meatballs are followed by feeding barium mixed with kibble if the dog has successfully emptied the barium-stained meatballs into the stomach. This feeding trial should help determine which food consistency is associated with the shortest esophageal transit time allowing the veterinarian to make nutritional recommendations to the pet owner.

Severely malnourished animals or animals suffering repeated bouts of aspiration pneumonia should have a temporary or permanent gastrostomy tube placed for enteral nutritional support. Gastrostomy tube feeding reduces the risk of aspiration pneumonia; however, dogs with ME can still aspirate saliva or ingesta refluxed from the stomach into the esophagus. Intermittent at-home suctioning of esophageal content via placement of a fenestrated esophagostomy tube for prevention of recurrent aspiration pneumonia is a viable consideration for dogs with a giant sigmoid esophagus.[27]

Hiatal Hernia and Gastroesophageal Reflux (GER)

Hiatal hernia is defined as any protrusion of abdominal contents (most commonly a portion of stomach) through the esophageal hiatus of the diaphragm into the thoracic cavity in the presence of an intact phrenico-esophageal ligament, and may occur as a congenital or acquired disorder in the dog. Congenital sliding hiatal hernias have been well documented in brachycephalic breeds. Their nasofacial conformation and unique respiratory anatomy predisposes these breeds to brachycephalic obstructive airway syndrome (BOAS), which increases negative intrathoracic pressure and causes subsequent hiatal herniation and GER during

Figure 4. A 2-year-old male neutered mix-breed dog with acquired idiopathic megaesophagus undergoing a swallowing fluoroscopic study while positioned in a Bailey chair to maintain the dog in an upright position and facilitate gravity-assisted feeding.

inspiration. Regardless of cause, hiatal herniation reduces LES pressure and leads to GER, esophagitis, and segmental or diffuse esophageal hypomotility.

Medical therapy should be implemented in animals with clinical signs of severe GER, esophagitis, and regurgitation before surgical intervention,[28] and is aimed at administering acid suppressants (proton pump inhibitors), diffusion barriers (sucralfate), and prokinetic agents (cisapride is preferred over metoclopramide) that also increase LES tone.[29] Dietary management comprises the feeding of a soaked kibble or canned fat-restricted diet (< 24% fat on ME basis) in smaller, more frequent meals throughout the day to facilitate gastric emptying; high-fat diets can delay gastric emptying in dogs.[30] Animals failing medical and dietary management may benefit from surgical management of BOAS with concurrent surgical reduction of the hiatal hernia.

CONCLUSION

Dietary modification plays a pivotal role in the management of dogs with dysphagia, and the anatomical categorization of the animal's swallowing impairment into oropharyngeal and/or esophageal causes followed by establishment of the underlying cause (structural vs. impaired motility) is important for optimizing dietary selection. Swallowing fluoroscopy and contrast static esophagrams are particularly helpful in dogs with ME for optimizing selection of food consistency. In general, increasing bolus viscosity from liquid to pudding consistency significantly reduces the prevalence of laryngeal penetration and aspiration in patients with oropharyngeal dysphagia. In contrast, there is no specific consistency of food that has been shown to be most reliable for facilitating esophageal transit in dogs with ME, underscoring the importance of contrast swallow studies in affected dogs. Dietary fat restriction should be implemented in dogs with hiatal hernia or increased GER. Severely malnourished animals or animals suffering repeated bouts of aspiration pneumonia should have a temporary or permanent gastrostomy tube placed for enteral nutritional support.

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HEPATIC DISEASES

HEPATIC DISEASE WITH OR WITHOUT HEPATIC ENCEPHALOPATHY IN DOGS

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KEY TAKEAWAYS

- Not every dog with hepatobiliary disease should be fed a commercial diet formulated for liver disease.
- Although excess dietary protein is ammoniagenic, severe protein restriction is not advised for dogs with hepatic encephalopathy.
- Dogs with copper-associated chronic hepatitis should be fed a copper-restricted diet for the rest of their lives.

INTRODUCTION

Hepatic disease, including chronic hepatitis (CH) and congenital portosystemic shunts (CPSS), can lead to a wide variety of accompanying clinical signs in dogs. These include hepatic encephalopathy (HE), portal hypertension, ascites, hemostatic disorders, and gastrointestinal signs. Nutritional management plays a role in treating several of these and is an important consideration for dogs with hepatobiliary disease.

ETIOPATHOGENESIS OF KEY CONDITIONS

Hepatic Encephalopathy

Congenital portosystemic shunts are the most common cause of hepatic encephalopathy in dogs. Alternatively, hepatic portal hypertension in dogs with advanced liver disease (e.g., chronic hepatitis) leads to the development of acquired portosystemic collateral vessels. Acute liver failure is a less common cause of HE in dogs.[1] Portosystemic shunting or hepatic failure can lead to ammonia dysmetabolism. This leads to astrocyte swelling, low-grade cerebral edema, and altered neurotransmission. Other factors such as systemic inflammation, manganese, oxidative stress, and various neurotoxins also play important roles.

Copper-Associated Hepatopathy

Copper is an essential trace element that is a cofactor for metallo-enzymes involved in various biochemical processes. The liver is the principal recipient of copper that is absorbed from the gastrointestinal tract. When the capacity of the hepatocyte copper-binding proteins is saturated, free copper ions lead to the formation of hydroxyl radicals which cause oxidative damage.[2] Copper can accumulate in the liver due to defects in copper metabolism, excessive dietary copper intake, or a combination of these factors. Cholestasis does not appear to be a major contributor to hepatic copper accumulation in dogs unless they are also exposed to a high dietary load.[3,4] Several breeds of dogs are predisposed to hepatic copper accumulation: Bedlington terrier, West Highland white terrier, Scottish terrier, Skye terrier, Labrador retriever, Dalmatian, and Doberman Pinscher.[5] It is also possible to see copper-associated CH in other dog breeds and in mixed-breed dogs.

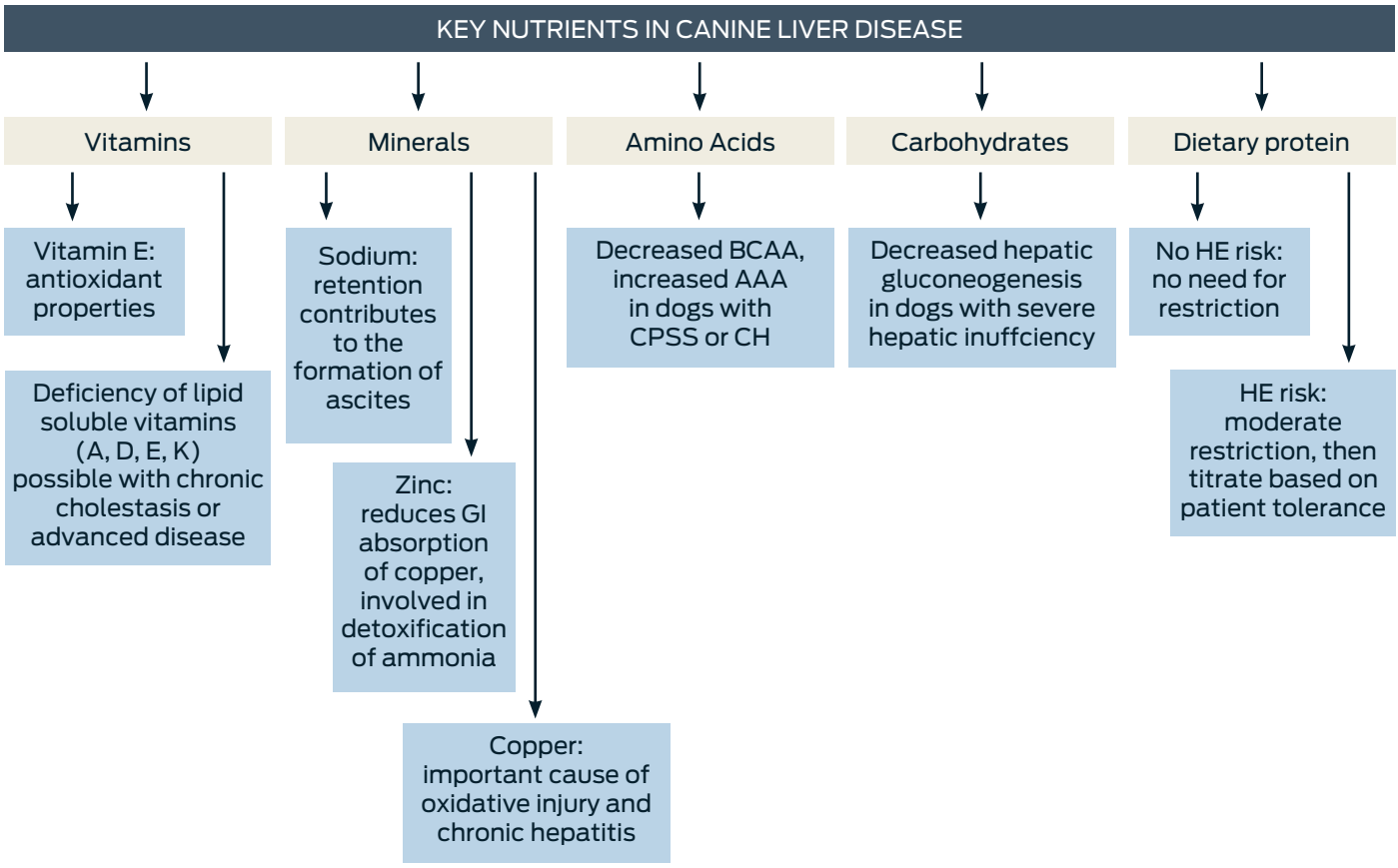
KEY NUTRIENTS (FIGURE 1)

Protein

Although excess dietary protein intake can lead to increased ammoniagenesis and therefore precipitate HE, long-term dietary protein restriction is not recommended in humans with HE. It is now recommended to initially restrict dietary protein and then to gradually feed more protein as long as the patient tolerates it. This helps maintain muscle mass and avoids contributing to a catabolic state.

The optimal protein requirements of dogs with CPSS or CH have not been determined, but similar recommendations to those for humans are now made. For dogs with HE, the amount of dietary protein recommended for an individual patient should be determined based on the diet history and the current protein intake, as well as the severity of clinical

Figure 1. Key nutrients in canine liver disease



HE = hepatic encephalopathy, BCAA = branch chain amino acid, AAA = aromatic amino acid, CPSS = congenital portosystemic shunt, CH = chronic hepatitis

signs. For a dog showing signs of HE while being fed a high-protein diet, decreasing dietary protein would be recommended, but a low-protein diet may not be necessary to reduce clinical signs.

Dogs with a CPSS or CH have been shown to have altered amino acid profiles compared with healthy dogs suggesting altered protein metabolism.[6,7] This is characterized by a decreased ratio of branched-chain amino acids (e.g., leucine, isoleucine, and valine) to aromatic amino acids (e.g., phenylalanine, tryptophan, and tyrosine). Aromatic amino acids have been purported to be involved in the pathogenesis of HE.[8]

Copper

Over the past 20 to 30 years there has been an apparent increase in the prevalence of copper-associated CH in dogs. The switch from supplementation with copper oxide, which demonstrated low bioavailability, to more bioavailable copper in commercial dog food has been hypothesized as a possible contributing factor.[9] The current AAFCO recommendation for minimum daily copper intake for maintenance adult canine diets is 0.183 mg/100 kcal (7.3 mg/kg dry matter; DM),[10] and the European Pet Food Industry (FEDIAF) recommended minimum daily intake is 0.180 mg/100 kcal (7.2 mg/kg DM).[11] There is no AAFCO maximum recommendation for copper. The FEDIAF nutritional guidelines describe a legal maximum for copper of 28.0 mg/kg DM (7.0 mg/1,000 kcal).[12] The legal maximum applies to any pet food to which copper is added as an additive and does not apply to diets without supplemental copper. Similar to AAFCO, FEDIAF have not established a nutritional maximum for copper.

The amount of copper in commercial dog foods is variable, and many foods greatly exceed the minimum limits. A study of 80 dry and 97 wet dog and cat foods from the United Kingdom found that > 9% had measured copper levels > 5 times the FEDIAF minimum. Additionally, 20% of foods analyzed were below minimum levels.[12] The copper in commercial dog foods comes from the mineral premix used as well as the other ingredients (which are usually animal-derived and may have varying copper contents over

time). Additionally, different forms of copper have very variable bioavailability. Treats and drinking water are other potential sources of this trace element that should be considered. Therefore, assessing the contribution of diet to copper-associated chronic hepatopathy in dogs is challenging, and further studies are needed.

Zinc

Zinc is another essential trace element that is important to consider in dogs with liver disease, especially copper-associated CH. This metal is a cofactor of several metalloenzymes and is involved in DNA synthesis, RNA transcription, and cell division. Zinc decreases the absorption of copper from the gastrointestinal tract and has been used to treat human patients with Wilson's disease.[13] Additionally, zinc is a cofactor for enzymes involved in the urea cycle, that converts ammonia to urea, and human patients with cirrhosis are often found to be zinc deficient.[14]

Fat-Soluble Vitamins

Bile acids play an important role in the emulsification of dietary fats and the formation of micelles in the small intestine. Therefore, patients with chronic cholestasis and other advanced liver diseases may be at risk of malabsorption of fats and fat-soluble vitamins (vitamins A, D, E, and K).[15] Vitamin K deficiency could contribute to coagulopathy in patients with hepatobiliary disease. Vitamin K1 supplementation is indicated in dogs with hepatobiliary disease that have chronic cholestasis as evidenced by a severely increased serum bilirubin concentration, acholic feces, or prolonged prothrombin times. Vitamin E has antioxidant properties, and deficiency is common in human patients with chronic cholestasis. Hypovitaminosis D is a negative prognostic indicator in humans with cirrhosis.[16]

COMMUNICATION TIP

While protein restriction has historically been recommended long-term for dogs with HE, it is now recommended to initially restrict dietary protein and then to gradually feed more protein as long as the patient tolerates it.

Sodium

Sodium is the primary determinant of extracellular fluid volume. In patients with ascites due to hepatic portal hypertension, activation of the renin-angiotensin-aldosterone system leads to the impaired renal excretion of sodium and a positive sodium balance. This perpetuates the formation of ascitic fluid.[17] Dietary sodium restriction has historically been recommended as the first-line therapy for human patients with ascites due to hepatic portal hypertension. However, the benefits of strict sodium restriction are controversial as it decreases the palatability of food and therefore increases the risk of malnutrition.[18] Another potential detrimental effect of sodium restriction is activation of the renin-angiotensin-aldosterone system.

DIETARY THERAPY

Hepatic Encephalopathy and Portosystemic Shunts

Dogs with HE are often fed commercial diets formulated for liver disease. These are moderately protein-restricted (typically 3.9–4.9 g/100 kcal) and have other characteristics including a non-meat-based protein source, reduced copper and sodium contents, supplementation with omega-3 fatty acids, supplementation with zinc, and inclusion of a blend of soluble and insoluble fibers (to help with digestive signs; **Box 1**).[1] The protein in these diets is of high quality (i.e., has a balanced amino acid profile and a relatively high bioavailability). As in humans, severe protein restriction is no longer recommended for dogs with HE as this can lead to protein malnutrition and muscle wasting. A diet based on dairy protein was less encephalogenic than one based on meat protein in dogs with portosystemic shunts.[19] In a study of dogs with CPSS fed two low-protein diets, one with meat and the other with soy, both diets decreased the severity of HE. However, improvements in ammonia concentrations and coagulation parameters were significantly greater in dogs fed the soy-based diet.[20] Therefore, non-meat protein-based diets are sometimes recommended for dogs with HE.

In practical terms, once the signs of HE are controlled with a commercial liver diet, it has been recommended to add small amounts of non-meat protein (e.g., soy protein or dairy protein) to the dog's diet to help prevent protein malnutrition.[20] Protein should not be

Box 1. Properties of and possible indications for commercial liver diets in dogs

Properties

- Moderate protein restriction
  - Typically, ~ 3.9–4.9 g/100 kcal
- Non-meat protein source
  - e.g., Soy protein
- High-quality protein source
  - Balanced amino acid profile and relatively high bioavailability
- Copper restriction
  - < 0.125 g/100 kcal
- Sodium restriction
- Zinc supplementation
- Long-chain omega-3 fatty acids
- Fiber-supplemented (soluble and insoluble blend)
  - Help with gastrointestinal signs

Potential indications

- Hepatic encephalopathy (treatment or prevention) *
  - Congenital portosystemic shunts
  - Acquired portosystemic shunts
  - Acute liver failure
- Copper-associated chronic hepatitis**
  - Initial treatment
  - Long-term maintenance

* Supplementation of non-meat-based protein sources should be considered on a case-by-case basis

** Supplementation of low-copper protein sources should be considered on a case-by-case basis

added at more than 10% of total daily calories to avoid nutritional deficiencies or excesses. Alternatively, a high-quality, highly digestible, moderate-protein diet designed for gastrointestinal disease, a complete and balanced vegetarian diet, a diet containing soy or dairy protein, or a diet appropriate for the patient's life stage can be used, provided the patient tolerates it. Avoiding unnecessary severe protein restriction applies to dogs at risk of HE (i.e., those documented to have congenital or acquired portosystemic shunts).[21] It is not uncommon for dogs to be diagnosed with CPSS when they are still growing, and it should be noted that commercial diets marketed for dogs with liver disease are not recommended for growing dogs. Whatever diet is fed, feeding small meals frequently may lessen the postprandial ammonia challenge.

Copper-Associated Chronic Hepatitis

Dogs with confirmed copper-associated CH should be treated with a chelating agent such as d-penicillamine. This drug removes copper from the liver by making it water-soluble so that it can be excreted in the urine. Administration of d-penicillamine is often associated with gastrointestinal side effects and is typically initially administered for at least 6 months. In addition, these dogs should be fed a copper-restricted diet for the rest of their lives. Commercial hepatic diets have copper contents < 0.125 g/100 kcal, below the AAFCO and FEDIAF minimum limits for maintenance diets. Additionally, these diets are supplemented with zinc, theoretically reducing the gastrointestinal tract's copper absorption. As these diets are moderately protein-restricted, which is not beneficial if the patient does not have HE or acquired portosystemic shunting, small amounts of low-copper protein sources (e.g., egg or cottage cheese, kept below 10% of total daily calories) can be added.[5] If the dog will not eat one of the commercial copper-restricted diets, a home-prepared low-copper diet can be formulated in consultation with a board-certified veterinary nutritionist.

Feeding a low-copper, high-zinc diet (0.125 mg copper/100 kcal and 6.43 mg zinc/100 kcal) without chelating agents resulted in a decrease in hepatic copper concentrations in a subset of clinically normal Labrador retrievers with previous hepatic copper accumulation.[22] However, in most dogs, initial treatment with d-penicillamine is recommended in addition to feeding a copper-restricted diet. The same diet was found to be helpful for maintenance therapy post-chelation in Labrador retrievers.[23] A third study in this breed did not find that the addition of zinc gluconate supplementation (200–250 mg/dog PO q12 hours) to copper restriction improved a diet's ability to decrease hepatic copper.[24]

The dog's intake of copper in water and any treats should also be considered. For water sourced from a well or in areas where piped water is known to have

a high content, copper concentrations should be analyzed (they should be < 0.10 µg/g).[5] Mineral water may be high in copper and should be avoided. In households with copper piping, it may be necessary to let the tap run for several minutes before filling the dog's bowl.

Once chelation therapy has been discontinued, some clinicians advise that supplementation with zinc acetate or zinc gluconate at a dose of 5–10 mg/kg of elemental zinc PO q12 hours is initiated. Plasma zinc concentrations should be measured during treatment to ensure that toxic concentrations (> 750–1,000 µg/dL; 115–153 µmol/L) are not reached.[5] Additional zinc supplementation should not be performed at the same time that d-penicillamine is administered. The efficacy of additional zinc supplementation has not been documented in dogs.

As excess hepatic copper leads to oxidative stress, there is a rationale for antioxidant therapy. S-adenosylmethionine (SAMe) is a precursor of the important hepatic antioxidant glutathione. At the recommended dose of 20 mg/kg PO q12 hours, SAMe has rarely been reported to have side effects in dogs other than occasional vomiting after dosing. Oral administration of SAMe has been shown to increase erythrocyte and hepatic glutathione concentrations but not improve histological changes consistent with vacuolar hepatopathy in dogs receiving prednisolone.[25] Studies evaluating the effect of this agent on clinical outcomes in dogs with CH have not been performed. Vitamin E is another antioxidant that protects cell and organelle membranes and is often given (α-tocopherol acetate, 10–15 IU/kg PO q24h) to dogs with copper-associated CH.[26] It is well tolerated, but its efficacy has not been studied in dogs with CH. Supplementation of antioxidants is also commonly initiated in dogs with a variety of other liver diseases. Products for which the purity and bioavailability in dogs have been independently verified should be used.

Idiopathic Chronic Hepatitis

Copper is not the only cause of CH in dogs, and sometimes an underlying cause is not found despite thorough diagnostic investigation. In a subset of these patients, autoimmunity is suspected to occur, and immunomodulatory therapy may be beneficial. The protein requirements of dogs with CH have not been well established, and protein restriction is not advised in the absence of HE. Not every dog with CH should be fed a commercial liver diet. The priority should be to ensure that dogs receive sufficient calories and nutrients by feeding adequate amounts of a palatable high-quality complete and balanced diet. It should be noted that some breeds of dogs are predisposed to copper-associated CH as well as immune-mediated hepatitis (e.g., Doberman Pinschers). In some cases, increased hepatic copper concentrations are present, but it is not clear they are leading to liver injury. Such patients should be evaluated on a case-by-case basis, but it may be most prudent to feed a copper-restricted diet to dogs with a hepatic copper concentration > 600 µg/g dry weight.[5]

Ascites Due to Hepatic Portal Hypertension

The optimal dietary sodium intake for dogs with ascites due to hepatic portal hypertension has not been established. As the value of sodium restriction in humans with this problem is controversial due to its negative effects on palatability and overall nutritional status as well as potentially leading to activation of the renin-angiotensin-aldosterone system, the safest advice is to avoid feeding these dogs a high-sodium diet (including treats).[5] Commercial hepatic diets are sodium-restricted.

Acute Liver Injury/Failure

Dogs with acute liver injury (without hepatic failure) do not need to be fed a liver diet. The priority should be to enterally provide sufficient calories and nutrients and a high-quality protein source (balanced amino acid profile and relatively high bioavailability). This can be achieved using a commercial diet for dogs with gastrointestinal disease.

Acute liver failure is defined as an acute liver injury with hepatic dysfunction (e.g., hyperbilirubinemia, coagulopathy, or HE). Dogs with acute liver failure are in a hypermetabolic state and have a negative nitrogen balance leading to catabolism. They are also predisposed to HE as they have a diminished capacity to detoxify ammonia.[21,27-29] Severe protein restriction is not needed, and a highly digestible commercial diet for gastrointestinal disease would be a good choice for many patients. For those with signs of HE, moderately protein-restricted diets, ideally with protein primarily coming from a non-meat source such as a commercial

diet for liver disease, have been advised.[21,27-29] Ensuring enteral nutrition may require using antiemetic drugs, appetite stimulants, or sometimes placing a feeding tube. Patients with acute liver failure have a reduced capacity for hepatic gluconeogenesis and are susceptible to hypoglycemia. They should therefore be fed diets with 30–50% of calories from easily digested complex, soluble carbohydrates such as rice, corn, wheat, or barley. Feeding small frequent meals may also help maintain euglycemia.[21,27,28]

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HEPATIC DISEASE WITH OR WITHOUT HEPATIC ENCEPHALOPATHY IN CATS

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KEY TAKEAWAYS

- Adequate nutritional support is important in the management and recovery of many types of feline liver disease.
- Hepatic encephalopathy can be a complication of some types of liver disease. Dietary management of hepatic encephalopathy involves limiting dietary protein intake.
- Dietary supplements may be beneficial in the management of some liver disorders.

DEFINITION

There are many types of liver disorders in the cat requiring specific medical, nutritional, and/or surgical management. Feline liver conditions can be simply grouped as congenital, inflammatory, acute toxic, neoplastic, or secondary reactive. (**Table 1** lists specific diseases and key therapies.) Each condition involves specific therapies, but all require appropriate nutritional support as part of the overall management. Hepatic lipidosis (HL), either idiopathic or occurring secondary to other disease, is a major liver disorder where nutrition is the primary therapy.[1] Some liver disorders may have the complication of hepatic encephalopathy (HE) which requires modifications in both diet and specific medical management.

PATHOPHYSIOLOGY

When liver disease becomes advanced, no matter the etiology, there will be a loss in the ability to carry out normal metabolic functions. The liver plays a central role in metabolism and utilization of carbohydrates, lipids, and protein as well as micronutrients, clotting factors, and albumin. The liver is also involved in metabolizing drugs and toxins and in the detoxification and excretion of products of metabolism.

Hepatic encephalopathy is a complex and poorly understood syndrome associated with formation of neurotoxins that impair neurotransmission. HE results when nitrogenous substances absorbed from the intestine undergo inadequate liver metabolism or when portal blood bypasses the liver, allowing offending substances to enter the brain. This produces alterations in neurotransmission affecting consciousness and behavior.[2] Ammonia is the key component associated with HE, but other gut-derived toxins also play a role in impaired neurotransmission. Alterations in the ratios of aromatic amino acids (AAA) to branched-chain amino acids (BCAA) in the brain are also thought to contribute to HE as increased concentrations of AAA promote the formation of false neurotransmitters.[3]

CLINICAL EVALUATION

The signalments and signs of cats with hepatic disease are variable. Most cats with chronic hepatic disease are middle aged or geriatric and often present with chronic hyporexia or anorexia, weight loss, and vomiting. Concurrent pancreatic and/or intestinal disease is common with inflammatory liver disease and may result in diarrhea. The involvement of the three together is referred to as feline triaditis.[4] Acute liver disease can occur at any age, and onset of signs may be related to ingestion of a hepatotoxin or medications. Signs for congenital disorders occur in younger cats. Physical examination findings of liver disease may include jaundice, muscle wasting, or hepatomegaly. Cats with congenital portosystemic shunts (PSS) are often stunted in size and may have copper-colored irises.[5] HE is uncommon but can occur with congenital PSS, hepatic lipidosis, acute liver failure, and occasionally from advanced chronic liver disease. Classic HE signs in cats are characterized by ptyalism, lethargy, behavior changes, and rarely seizures.[2]

Laboratory evaluation, imaging studies, and liver biopsy are required to identify a specific liver disease.

Table 1. Common feline liver diseases and key therapies involved in their management

Classification	Key therapies	Requires HE therapy?
Degenerative		
Hepatic lipidosis	Nutrition	Occasionally
Reactive hepatopathies	Supportive care	Rare
Inflammatory		
Neutrophilic cholangitis	Antibiotics	Occasionally
Lymphocytic cholangitis	Immunomodulation	Occasionally
Necrosis (extensive)		
Acute hepatic toxicity	Supportive/antioxidants	Common
Congenital		
Portosystemic shunt	Surgery/supportive	Common
Ductal plate anomalies van Meyenburg complex Caroli's disease	 Supportive Supportive	 Common Rare
Neoplasia		
Primary hepatic	Surgery/chemotherapy	Rare
Non-primary hepatic	Surgery/chemotherapy	Rare

Elevations in liver enzymes reflect liver involvement but are variable depending on the type and extent of disease. Elevation in total bilirubin is common in feline liver disease, and presence of clinical icterus, without hemolytic disease, suggests a primary hepatobiliary disorder. Other biochemistry changes are variable and with advanced hepatic dysfunction may include hypoglycemia, low blood urea nitrogen, or coagulation abnormalities. Urinalysis may reveal bilirubinuria. Serum bile acids are abnormal in cats having portosystemic shunting or significant hepatic dysfunction. Abnormal elevation in serum ammonia (NH_3) concentrations supports HE.[2]

Ultrasonography findings help characterize the type of liver disease. Ultrasonography is very useful to evaluate the liver parenchyma, biliary system, and vascular system. Ultrasound-guided fine needle aspirate with cytology showing lipid-laden hepatocytes supports the diagnosis of hepatic lipidosis. Cytology may identify neoplasia or other liver disorders, but a liver biopsy is required for a definitive diagnosis of hepatic parenchymal disease.[6] CT angiography may be required to identify PSS.

MEDICAL MANAGEMENT

Treatment should begin first with patient stabilization by correcting fluid and electrolyte alterations, as well as hypoglycemia, if present. With nausea and/or vomiting, antiemetic therapy is indicated. Maropitant is the author's first choice antiemetic. Ondansetron is an alternative broad-spectrum antiemetic. Metoclopramide is considered a poor choice in

cats because of weak antiemetic and prokinetic properties due to the cat's lack of dopamine receptors.[7] Mirtazapine, a commonly used appetite stimulate, also has antiemetic and prokinetic properties.[8] Gastrointestinal ulceration is treated with proton pump inhibitors such as omeprazole and/or the oral gastroprotectant sucralfate. Coagulopathies may occur in advanced hepatic disease, but spontaneous bleeding is unusual. Vitamin K1 treatment is indicated when there is bleeding or before performing invasive procedures.[9] Although ascites is an uncommon consequence in cats, diuretic therapy using spironolactone is most effective in managing ascites secondary to liver disease. With acute hepatotoxicity, antioxidant support is often used. N-acetylcysteine (NAC) is suggested in advanced hepatic failure.[10] NAC increases hepatic glutathione concentrations protecting against oxidative stress and also has other hepatoprotective properties.[11]

Although HE is uncommon in the cat, important medical and nutritional therapy should be initiated if HE is suspected and confirmed by elevated ammonia (NH_3) concentrations. First, it is important to identify and eliminate all precipitating factors that may initiate HE (see **Box 1**).[2] Fluid therapy corrects fluid deficits, as well as electrolyte and acid–base abnormalities, and improves renal function. The management next involves decreasing GI absorption of NH_3 and other nitrogenous substances causing HE. Oral lactulose is a nonabsorbable carbohydrate that inhibits intestinal NH_3 production by acidification of the gut lumen that favors conversion of ammonia (NH_3) to poorly absorbed ammonium (NH_4), essentially trapping NH_3 within the gut lumen.[2] Gut acidification inhibits ammoniagenic coliform bacteria and also works as a cathartic, reducing colonic bacterial load. Lactulose can also be given by enema in treating a severe case of hepatic encephalopathy in a patient unable to take oral medication.[12] Intestinal antibiotics such as neomycin or metronidazole may be added to suppress urease-producing organisms.

Box 1. Precipitating factors associated with hepatic encephalopathy

- Gastrointestinal bleeding
- Infection
- Medications
- Constipation
- Alkalosis
- Hypokalemia
- Malnutrition
- Dietary protein overload

NUTRITIONAL MANAGEMENT

Assuring adequate nutritional intake is an important part of hepatic therapy, and a complete nutritional assessment is required to determine the patient's needs. The goal is to provide appropriate nutrition for the patient with liver disease without stressing the liver's metabolic capacity. Liver disease is often associated with anorexia and vomiting, resulting in negative energy intake and weight loss. If the patient fails to meet their nutritional needs, enteral nutritional replacement should be initiated. Increasing diet palatability and/or appetite stimulants such as mirtazapine or capromorelin may work for mild cases, but enteral nutritional replacement with tube feeding is generally required for more severe cases.[8,13] The reader should refer to the chapter on Hepatic Lipidosis in Cats and the Practical Tool on Assisted Feeding and Using Feeding Tubes for a detailed description on tube feeding, indications, and management.

Nutritional Assessment

The patient should have an accurate body weight recorded and a body condition score (BCS) determined. Muscle wasting can make body condition scoring more difficult. Determining a muscle condition score (MCS; rated as normal muscle mass or mild, moderate, or severe muscle wasting) based on palpation is helpful when formulating the nutritional assessment. Feeding amount is based on resting energy requirements (RER) for their current or estimated ideal body weight while in the hospital and their estimated ideal body weight when at home. Calculation of RER = 70 x (BW in kg)$^{0.75}$.

Key Nutrients

The key nutrients for managing liver disease in cats are protein and fat. Cats have a high protein requirement being obligate carnivores, and significant cachexia can result from inadequate protein intake during periods of anorexia.[14,15] Protein therapy corrects the negative nitrogen balance resulting from anorexia and provides essential amino acids. Adequate energy is required to meet needed RER levels, and fat efficiently provides

that energy in a small feeding volume when given with adequate protein supplementation. Approximately 35–45% of the diet's metabolizable energy should come from protein, provided HE is not present. Carbohydrates are less important as a caloric source for cats, and high carbohydrate diets should be avoided.[4] Providing a complete and balanced diet that is protein rich, with fat as a major energy source and limited carbohydrates is recommended for cats without HE.

Hepatic Encephalopathy

HE results from the abnormal uptake of nitrogenous substances derived from dietary proteins in the GI tract that enter the brain and alter the normal neurotransmission system. Dietary protein restriction below the minimum amount recommended by AAFCO or FEDIAF is often incorrectly recommended for patients with HE in hopes of decreasing intestinal ammonia production. Protein-restricted diets are inappropriate in cats because protein is a major source of energy and adequate caloric intake is essential to prevent weight loss and amino acid deficiency. The lack of appropriate dietary protein results in loss of muscle mass, which reduces extrahepatic ammonia removal. Muscles store up to 50% of body ammonia, and muscle wasting potentiates hyperammonemia and HE.[16] Protein restriction in HE should not be lower than minimum values determined for cats with chronic renal insufficiency (approximately 5.75–10 g/100 kcal where AAFCO minimum for adult maintenance is 65 g/1000 kcal or 6.5 g/100 kcal and the FEDIAF minimum recommended level for adult cats is 62.5 g/1000 kcal or 6.25 g/100 kcal [100 kcal/kg$^{0.67}$]).[3,17,18] Veterinary therapeutic hepatic or renal diets often meet or are slightly below AAFCO and FEDIAF minimum requirements, providing a high quality, highly digestible protein source and supplying essential amino acids. Renal diets are also phosphorus restricted, so cats with HE, especially growing kittens, fed renal diets for protein restriction should be monitored carefully. Different cats with HE tolerate different levels of protein, and the dietary protein concentration should be tailored to what the cat can tolerate without developing clinical signs.

COMMUNICATION TIP

"Although HE is uncommon in the cat, important medical and nutritional therapy should be initiated if HE is suspected and confirmed by elevated ammonia (NH_3) concentrations."

Alterations in the ratios of aromatic amino acids (AAA) to branched-chain amino acids (BCAA) in the brain are also thought to contribute to HE. Plant-based and dairy proteins are preferable to red meat proteins as they provide a higher calorie to nitrogen ratio and tend to be higher in BCAA than in AAA.[2,3]

Supplements

Vitamins and micronutrients as well as other alternative supplements have been suggested for cats with liver disease. Box 2 in the chapter on Hepatic Lipidosis in Cats lists supplements suggested by various authors. Many lack critical scientific evaluation showing a benefit for cats with liver disease. Because cats have a high requirement for essential amino acids and the inability to conserve methionine, taurine, and arginine, some recommend these for additional supplementation.[19] Arginine deficiency in cats can cause rapid development of HE, and taurine is essential for bile acid conjugation.[3,20] L-carnitine is an essential cofactor for transport of long-chain fatty acids into mitochondria and was also found to improve HE symptoms by unknown mechanisms in humans.[16,21] Veterinary therapeutic feline diets often contain adequate amounts of these micronutrients. Since B vitamins are involved as co-factors in hepatic metabolism, cats with liver disease may require additional supplementation.[3] Critically ill cats are especially susceptible to cobalamin (B12), and vitamin K1 deficiency.[9,22] Oxidative damage plays a role in liver disease, and antioxidant supplements and other liver support therapy is often recommended.[23] Supplements such as antioxidants (vitamin E), nutraceuticals (s-adenosylmethionine [SAMe]), and herbals (silymarin) are often prescribed for liver support.[3,24] Prebiotics, probiotics, or synbiotics have also been shown to increase non-urease-producing *Lactobacillus* species with a decrease in urease-producing bacteria and may be helpful in chronic HE management.[25]

Feeding Management

If the cat with liver disease is unable to consume a complete and balanced diet meeting calculated energy requirements, then a feeding tube should be placed to provide those needed nutritional requirements. Adequate feeding also prevents formation of secondary HL that can occur in conjunction with other types of liver disease. Either an esophagostomy (E), nasogastric (NG), nasoesophageal (NE), or gastrostomy (G) feeding tube should be placed. Using a critical care-type energy dense, high protein and high fat diet designed for easy tube feeding or a canned balanced veterinary therapeutic feline diet is appropriate for tube feeding. With HE, a lower protein formulated hepatic or renal diet should be used. The calculated feeding amount should be divided into 4 or more feedings per day. Small frequent feedings optimize hepatic assimilation of nutrients. Since feeding using the total calculated RER is rarely tolerated initially, the amount fed should be gradually increased over a period of approximately 4 or more days to reach the calculated RER. For example, 25% on day one, then 50% on day two, then 75% on day three, and so on. Slow introduction to food also helps prevent complications, including vomiting, nausea, glucose and electrolyte imbalances, and, in more severe cases, refeeding syndrome. In some cases, tube feeding may cause vomiting and discomfort that requires feeding even smaller volumes with increased frequency (such as 6–8 feedings a day). Once the patient is stable and feeding is tolerated, the patient can be released to the owner for home care, including tube feeding and continued medical care. The owner should also encourage voluntary food intake by offering various types of enticing but nutritionally appropriate foods prior to each tube feeding. A complete and balanced home-cooked diet can be formulated by a board-certified veterinary nutritionist, but acceptance of home-cooked diets can be low in cats. Appetite stimulants should also be considered. The feeding tube is only removed once the cat is reliably eating a nutritionally balanced diet.

PROGNOSIS

The prognosis for feline liver disease depends on the specific disease and the response to medical or surgical management. Severely debilitated or very aged cats or those with advanced liver failure have a poorer prognosis. Providing a complete and balanced feline diet that is energy dense and protein rich (or lower but adequate in protein if HE is present), with fat as a major energy source is important in the recovery. Liver disease coupled with inadequate nutritional intake could lead to the development of secondary hepatic lipidosis, which becomes a complicating factor in patient recovery.

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HEPATIC LIPIDOSIS IN CATS

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KEY TAKEAWAYS

- Hepatic lipidosis is a syndrome unique to the cat resulting from anorexia with protein-calorie malnutrition.
- Providing appropriate nutritional support using enteral feeding tubes to correct nutritional deficiencies can result in return to normal hepatic function.
- Hepatic lipidosis is either idiopathic or occurs in association with another underlying disease process requiring a thorough diagnostic investigation.
- The prognosis is good if diagnosed early, aggressive therapy is initiated, and underlying disease managed.

DEFINITION

Hepatic lipidosis (HL) is a syndrome associated with protein-calorie malnutrition resulting in excessive accumulation of lipid within hepatocytes leading to hepatic dysfunction. HL is either idiopathic and associated with unexplained anorexia, usually from stressful events, or as a complication of another primary disease resulting in prolonged anorexia. Most authors believe a majority if not all cats with HL have some other primary disease. However, one large case series found 28% to be likely idiopathic.[1] **Box 1** lists common conditions that have been associated with secondary hepatic lipidosis.[2] Severe hepatic lipid accumulation may result in a potentially fatal intrahepatic cholestatic liver disease. Successful treatment involves aggressive nutritional support, correction of metabolic derangements and addressing any underlying disease. Hepatic lipidosis is a reversable condition if identified early and nutritional deficits are corrected.

Box 1. Some underlying disease conditions associated with hepatic lipidosis in cats

- Acute and chronic pancreatitis
- Inflammatory bowel disease
- Alimentary lymphoma
- Cholangitis
- Hepatic neoplasia
- Other liver disorders
- Diabetes mellitus
- Hyperthyroidism
- Chronic kidney disease
- Urolithiasis
- Cardiopulmonary disease
- Other neoplasia

PATHOPHYSIOLOGY

The pathophysiology of HL is complex and poorly understood. HL is also unique to the cat and has not been recognized as such in the dog. The cat's high protein requirements coupled with derangements in normal lipid metabolism are thought to result in hepatic lipid accumulation from prolonged inappetence.[3] Anorexia with protein-calorie malnutrition results in peripheral lipolysis with free fatty acid release into the circulation and delivery to the liver. When fatty acid delivery exceeds the hepatocyte's ability to oxidize fatty acids for energy or to secrete them back in the circulation as very-low-density lipoproteins, fatty acids are converted to triglycerides (TG) and stored in the hepatocyte.[4] The excessive accumulation of hepatic TG is the hallmark of HL, and lipid accumulation can disrupt normal hepatic function. Protein malnutrition with marked muscle wasting are features of the HL syndrome, and it is speculated that specific protein deficits likely also contribute to derangements in lipid metabolism. Correction of nutritional deficiencies results in reversal of hepatic TG accumulation and a return to normal hepatic function.

CLINICAL EVALUATION

Most cats with HL are middle aged or older and are or have a history of being overweight or obese. Classical clinical signs are typically present for a relatively short period of time (days to several weeks) and include anorexia, significant weight loss, and lethargy. The initiating event for anorexia may be certain stress factors or an underlying disease. Other signs are variable including nausea, vomiting, and salivation. Physical examination may reveal weakness, dehydration, jaundice, hepatomegaly, and muscle wasting. Characteristically there is significant loss of muscle mass while inguinal and intra-abdominal fat stores are often spared.[5,6]

Laboratory testing and imaging studies are required in diagnostic workup of suspected HL. Characteristic laboratory findings of HL include a nonregenerative anemia with poikilocytosis and Heinz bodies reflecting oxidative stress.[5] Key serum biochemical abnormalities that reflect intrahepatic cholestasis include marked increases in total bilirubin and alkaline phosphatase (ALP) activity and variable increases in alanine aminotransferase (ALT) and aspartate aminotransferase (AST) activities. A typical feature of HL is that γ-glutamyltransferase (GGT) activity, also a cholestatic liver enzyme, is inconsistent and often normal likely because GGT activity better reflects extrahepatic cholestasis and less so intrahepatic cholestasis.[5] Other biochemistry changes are variable and may include hyper- or hypoglycemia, low blood urea nitrogen, hypokalemia, hypophosphatemia, or hypomagnesemia. Forty-five percent of HL cats are reported to have coagulation abnormalities as the result of vitamin K deficiency.[7] Urinalysis may reveal bilirubinuria, ketonuria, or lipiduria. Additional testing should include measurement of pancreatic lipase as acute pancreatitis can resemble HL, and serum folate and cobalamin as cats with HL often have intestinal disease that may alter these B vitamin concentrations.[8]

Ultrasonography findings include hepatomegaly with diffuse hyperechogenicity of the liver parenchyma.[9] Ultrasound-guided fine needle aspirates with cytology show a majority of hepatocytes with cytosolic vacuolization containing lipid.[10] These findings with the clinical, laboratory, and imaging findings generally is all that is required for a clinical diagnosis of HL. Rarely a liver biopsy with histopathology is needed to make the diagnosis but may help determine if there are other concurrent hepatic disorders.

THERAPY OF HEPATIC LIPIDOSIS

The management of HL is three-fold: 1) identify and treat any specific underlying disease occurring as major comorbidity, 2) medical management treating metabolic abnormalities and complications associated with underlying disease, and 3) nutritional management. Prompt and aggressive therapy is required for a successful outcome.

Medical Management

Treatment should begin with patient stabilization by correcting fluid and electrolyte alterations. Most patients are critical, and intravenous fluid therapy is advised using balanced crystalloid fluids to replace fluid deficits and to provide daily maintenance requirements. Glucose-containing fluids should be avoided because most HL cats exhibit glucose intolerance.[6] Electrolyte abnormalities such as hypokalemia, hypophosphatemia, and hypomagnesemia should be corrected.

With nausea and/or vomiting, antiemetic therapy is indicated. Maropitant is the author's first choice antiemetic. It is a broad-spectrum antiemetic that also blocks visceral pain. Ondansetron is an alternative broad-spectrum antiemetic, and occasionally it is used alone or in combination with maropitant if vomiting is difficult to control. Metoclopramide is considered a poor choice because it should be given by constant rate infusion and has both weak antiemetic and prokinetic properties in cats. Additionally, metoclopramide is a dopamine antagonist. Dopamine therapy has been shown to protect against experimental hemorrhagic pancreatitis in cats and pancreatitis is associated with HL.[11] Mirtazapine, a commonly used appetite stimulant, has antiemetic and prokinetic properties as well.[12]

Other medical therapy should be prescribed on an individual basis. Antacid therapy (famotidine, pantoprazole, or omeprazole) is indicated if gastric ulceration or reflux esophagitis is suspected. If gastric hypomotility complicates oral nutritional therapy, the prokinetic cisapride may be beneficial. Coagulopathies are common with HL, but spontaneous bleeding is not. Vitamin K deficiency is generally the cause of most coagulopathies in HL, and vitamin K1 treatment is indicated when there is bleeding or before performing invasive procedures.[7] Hepatic encephalopathy (HE) is uncommon in HL. Lastly, some authors suggest N-acetylcysteine (NAC) be given in cats with HL and

advanced hepatic failure.[2] NAC is a sulfhydryl group donor, increasing hepatic glutathione concentrations protecting against oxidative stress. NAC is also reported to have additional hepatoprotective properties in hepatic failure in humans, but studies particularly looking at feline HL are lacking.[13]

Nutritional Management

Enteral nutrition is the most critical aspect of therapy for feline HL. Enteral nutritional replacement should begin immediately and is accomplished using feeding tubes. One should not rely on voluntary intake, and force feeding should also be avoided as it rarely achieves adequate caloric intake, adds undue stress to the patient, and may cause food aversion. Appetite stimulants may work in early mild cases but are most beneficial when attempting to initiate voluntary intake later in the nutritional support. Mirtazapine (transdermal) and capromorelin, a ghrelin receptor agonist, (oral liquid) are examples of appetite stimulants that are approved for use in cats.[12,14]

COMMUNICATION TIP

"Even though many cats with HL are overweight or obese, the goal is to approximately maintain body weight during the recovery period, and to focus on restoring health prior to implementing a weight loss plan."

Nutritional assessment: The patient should first have an accurate body weight recorded and be assigned a body condition score (BCS). Muscle wasting can make body condition scoring more difficult. Determining a muscle condition score (MCS; rated as normal or as mild, moderate, or severe muscle wasting) based on palpation is helpful in formulating the nutritional assessment. Any nutritional intake should also be recorded as to type and amount. Cats with HL are usually fed based on RER for their current or estimated ideal body weight in the hospital and their estimated ideal body weight at home. Their resting energy requirements (RER) = 70 x (BW in kg)$^{0.75}$.

Key nutrients: The key nutrients for managing HL in cats are protein and fat. Cats have a high protein requirement being obligate carnivores, and significant sarcopenia resulting from inadequate protein intake occurs during periods of anorexia.[3,15] Protein therapy corrects the negative nitrogen balance and replaces essential amino acids resulting from anorexia. Adequate energy is required to meet needed RER levels, and fat, being the most energy-dense nutrient, efficiently provides that energy when given with adequate protein supplementation. Approximately 35–45% of the diet's metabolizable energy should come from protein. Feeding high-fat diets with adequate protein will not increase hepatic lipid accumulation.[5] Carbohydrates are less important as a caloric source for cats, and high carbohydrate diets should be avoided.[6] A complete and balanced feline diet that is energy dense, protein rich, has fat as a major energy source, and with limited carbohydrate content is recommended for cats with HL.[5]

Supplements: Box 2 lists various micronutrients and supplements that have been recommended by various authors.[5,6] Justification includes the cat's higher requirement for essential amino acids and inability to conserve methionine, cysteine, taurine, and arginine during prolonged anorexia. Cats with HL also have concurrent oxidative damage suggesting a need for antioxidant therapy.[16] Supplement recommendations are primarily anecdotal as there are no strong, controlled studies demonstrating the importance of most of these micronutrients or supplements in improving the recovery of feline HL. There is, however, some compelling evidence that some cats with HL have low serum cobalamin concentrations and deficient cats benefit from additional cobalamin supplementation.[5,17] Providing various supplements is at the discretion of the clinician.

Feeding management: Feeding tubes are required to supply adequate nutrition. Esophagostomy (E) tubes and nasoesophageal (NE) or nasogastric (NG) feeding tubes are commonly used. Gastrostomy feeding (G) tubes are placed during surgery or by endoscopy, are more expensive, and have more serious complications. The reader should refer to techniques describing tube placement and management. NE and NG tubes are placed without general anesthesia and used in hospitalized critical cases before a larger feeding tube can be safely placed, once the patient is stable enough for general anesthesia.[18] Liquid diets with high protein

Box 2. Supplements and micronutrients that have been suggested in the management of feline hepatic lipidosis. For many listed, there is little or no evidence of proven benefit in treating hepatic lipidosis

- Arginine
- Taurine
- L-carnitine
- Thiamine
- B-complex vitamins
- Cobalamin
- Vitamin E
- S-adenosylmethionine
- Silybin
- N-acetylcysteine

and high fat concentrations formulated for cats should be used for feeding with a small diameter NE or NG tube. NE or NG feeding is done by slow pulse (bolus) feeding or by constant rate infusion. E tubes are the ideal way to feed cats with HL long-term, and once the cat is stable enough for anesthesia, an E tube should be placed. Placement of the larger diameter feeding tubes allows using canned calorie-dense diets. Critical care-type high energy diets are designed for easy tube feeding. Other canned complete and balanced veterinary therapeutic feline diets are also appropriate depending on the underlying disease or concurrent medical conditions. These canned diets will require mixing with water (approximately 30 to 90 mL for a 5.5–6 ounce or 150–200 gram can) or a liquid diet so that they can easily be passed through the E or G tube.[6] Feeding should be slow, over 10–15 minutes, and one should monitor for signs of discomfort or nausea such as drooling or licking of the lips. If signs are observed, one should temporarily stop the feeding and resume when the cat is comfortable. Occasionally it may be necessary to manage nausea or vomiting with antiemetic therapy.

Dietary instructions: Once the daily amount to be fed is calculated, that amount should be divided into 4 or more feedings per day. Attempting to feed the total calculated RER on day one rarely is tolerated, and consequently the amount fed should be gradually increased over a period of approximately 4 days to reach the calculated RER. For example, 25% on day one, then 50% on day two, then 75% on day three, and so on. If the patient has complications, clinicians should increase calories more slowly. In some cases, feeding may cause vomiting and discomfort that requires feeding even smaller volumes with increased frequency (such as 6–8 feedings a day). Lastly, prokinetic therapy may be required if gastric hypomotility is thought to be responsible for the nausea and vomiting. Once the patient is stable and feeding is well tolerated, the patient can be released to the owner for home care. The owner must be instructed on feeding and tube care. The owner should also encourage voluntary food intake when at home by offering various types of enticing foods prior to each feeding. This is also when appetite stimulants should be considered. The feeding tube is only removed once the cat is reliably eating its RER with a nutritionally balanced diet. The duration of tube feeding is quite variable usually lasting 3–6 weeks, or potentially longer if concurrent diseases are present.

A rare complication is refeeding syndrome. This usually only occurs in the very debilitated cats having undergone prolonged anorexia. This syndrome results as a response to feeding with a rapid release of endogenous insulin promoting cellular uptake of glucose, phosphate, potassium, and magnesium.[19] It is important to recognize these shifts and to institute appropriate fluid and electrolyte therapy if they should occur, in addition to reducing the rate at which the patient is increased to RER.

PROGNOSIS AND MONITORING

The prognosis for HL is dependent on several factors: early initiation and success of nutritional therapy, concurrent underlying disease, and general condition of the patient. An additional variable is the owner's willingness to be involved in the management of their pet at home. Recovery rates range from approximately 60% to as high as 92%.[1,5,6] The high survival rates reported have excluded those with fatal secondary disease. The prognosis is poor for cats in hepatic failure or with severe debilitation or advanced age.[1] In the absence of serious concurrent disease and with successful nutritional support the prognosis can be good even in cases having an underlying disease.[1] Hepatic lipid accumulation is a reversable process, and once recovered very few if any cats ever develop recurrence of HL.

During the recovery period, cats should be assessed for voluntary food intake, body weight, BCS, and MCS every 1–2 weeks. Even though many cats with HL are overweight or obese, the goal is to approximately maintain body weight during the recovery period, and to focus on restoring health prior to implementing a weight loss plan. Once the cat is healthy, the tube has been removed, and the cat is voluntarily eating an adequate amount, weight loss can be considered.

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PRACTICAL TOOL: RECOMMENDATIONS FOR DIETARY MANAGEMENT OF LIVER DISEASE

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The primary goals of nutritional management of dogs and cats with liver disease include 1) selecting dietary modifications based on disease etiology and clinical signs, 2) ameliorating clinical signs, and 3) meeting the nutrient requirements of the patient while supporting liver regeneration.[1] Dietary modification should only be implemented after an individualized nutritional assessment. Stable patients with hyporexia or anorexia may benefit from placement of assisted feeding devices (e.g., esophagostomy tube) early in the disease process to help provide complete and balanced nutrition, medications, and fluid supplementation. Nutritional supplements such as vitamin E, vitamin C, SAMe, silymarin, and L-carnitine may also be beneficial for patients with liver disease.[1]

Table 1. Selected dietary considerations for dogs and cats with liver diseases

Nutrient of concern	Management considerations	Conditions and suggested dietary modifications
Energy	• Requirement may be increased due to catabolic disease • Goal: maintain or increase body weight, body condition score, and muscle condition score during treatment depending on nutritional assessment	• Underweight patients: energy-dense diet ≥ 3800 kcal/kg • Consider dividing total intake into four to six small meals per day, especially for patients with hepatic encephalopathy (HE)
Fat	• Prolonged anorexia can result in metabolic shifts favoring high fatty acid utilization[1]	• Hepatic lipidosis (HL): consider recovery-type diets with high fat content (>6 g fat/100 kcal) • Most patients: provide 3–5 g fat/100 kcal for dogs and 4–6 g fat/100 kcal for cats for energy density and palatability • Note: high fat diets (>4 g fat/100 kcal for dogs) contraindicated in patients with severe cholestatic disease[1]
Protein	• Utilized for maintenance of lean muscle mass and protein synthesis • Should NOT be restricted unless clinical signs of HE are present	**WITH HE:** • Initial reduction of protein intake by 25% from current level then re-evaluate • Ensure adequate intake of essential amino acids (e.g., taurine, arginine in cats)[1] • Consider use of plant-based/dairy proteins[2] • If restriction below AAFCO or FEDIAF minimum recommendation is necessary and/or if the patient is growing, consult with a Board-Certified Veterinary Nutritionist® **WITHOUT HE:** • Meet or exceed AAFCO and/or FEDIAF minimum recommended amounts

Digestible Carbohydrate	· Hepatopathies may result in derangements in digestible carbohydrate metabolism[1]	Can vary digestible carbohydrate intake (initially up to 25% increase or decrease) as indicated, and then re-evaluate patient: - Consider increases with: cirrhosis, vascular anomaly, hepatic failure, hypoglycemia, hepatic neoplasia[3] - Consider decreases with: HL, hyperglycemia, patients at risk for refeeding syndrome[4]
Soluble Fiber	· May reduce clinical signs of HE through nitrogen trapping and reduction of ammonia absorption[1]	HE: · Psyllium husk dose: 1/8 tsp (approximately 0.5 g) per 4.5 kg (10 lb) body weight, twice daily May increase depending on patient tolerance[1]
Copper	· Hepatic copper accumulation causes oxidative damage to the liver when not bound to protein · Dietary copper restriction is not necessary in dogs without hepatic copper accumulation	Copper-associated hepatopathy (CAH): · Long-term management with an otherwise complete and balanced reduced copper diet (<0.125 mg/100 kcal)[3]
Zinc	· Supplementation may reduce intestinal copper absorption and reduce liver copper accumulation[5] · Deficiency may occur secondary to liver disease[3]	CAH patients: · 15 mg/kg elemental zinc as a copper chelator (induction dose followed by taper)[5] Non-CAH patients with deficiency: · 1–3 mg/kg elemental zinc per day[4]
Vitamin K, B Vitamins	Deficiencies common in liver disease	If deficiency suspected, supplement Vitamin K1 (phytonadione) and/or B-complex

*Suggested nutrient levels based on publications. Recommended dietary modifications may be applicable generally to patients with liver disease unless otherwise indicated.

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PURINA Institute

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JOINT DISEASE

OSTEOARTHRITIS IN DOGS

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KEY TAKEAWAYS

- There is evidence that nutritional modification can be used in dogs with OA, and the effects of the nutritional agent on pain or disease progression over time must be considered when designing a nutritional plan.
- There are multiple dietary strategies available for OA in dogs; however, a multimodal approach including diet, exercise, and rehabilitation may provide the best outcome long-term.
- Weight management and omega-3 fatty acid supplementation have extensive research to support use in dogs with OA.

INTRODUCTION

Osteoarthritis (OA) or degenerative joint disease is a progressive degeneration of diarthrodial synovial joints which results in articular chondrocyte death, synovial inflammation, loss of normal joint fluid and cartilage, subchondral bone sclerosis, osteophyte and enthesophyte formation, and ultimately loss of joint function and chronic maladaptive pain.[1,2] OA is very prevalent in dogs, with approximately 1 in 5 adults affected.[3] While the disease is incurable, significant reduction in its progression over time is achievable.

Treatment of OA is aimed at reducing pain and lameness, improving mobility and activity, and improving quality of life by slowing the progression of degeneration.[4,5] A multimodal approach has been recommended with treatment including physiotherapy, diet restriction, oral nutraceutical supplementation, and pain management.[6-8] In the past, treatment of OA in companion animals has focused on controlling the pain associated with the disease, rather than on its progression over time; however, with an aging human population, demand for improved quality of life in aging pets has become a priority. Greater than 90% of dogs over 5 years of age may be affected by osteoarthritis.[9,10] The goal of nutritional management of OA must encompass two divisions: one focusing on pain management and the other on helping reduce progression of the disease over time. This chapter provides current scientific evidence regarding the most common and widely available nutritional strategies and supplements for OA. Additional supplements may be available in some countries, and veterinarians are encouraged to make recommendations using an evidence-based approach.

NUTRITIONAL MANAGEMENT OF OSTEOARTHRITIS DISEASE PROGRESSION IN DOGS

OA progression and continued degradation of the synovial joint is the result of a complex association of factors within the chondrocytes of articular cartilage and the joint's synovial cells.[11,12] Modification of these pathways and maintaining chondrocyte health must remain a priority if the management of OA is to be successful in the long term. Unfortunately, most veterinary clinical trials fail to provide long-term outcome of nutritional interventions in dogs with OA, therefore evidence of effectiveness on progression of OA is limited. Nutritional interventions will be summarized with respect to their effects on OA progression over time.

NUTRITIONAL MANAGEMENT OF PAIN AND LAMENESS IN OA IN DOGS

One of the most important and well-researched aspects of OA is pain and lameness. Quality of life is severely affected by progression of this disease and may be life-limiting in some individuals.[13,14] Pain management has therefore been a major component of OA treatment and NSAIDs have traditionally been the focus in dogs with OA; however, NSAIDs and corticosteroids may have adverse effects on gastrointestinal, renal, and hepatic

systems, and may accelerate cartilage degeneration with long-term use.[15-17] Diet and nutraceutical supplements offer an opportunity to help manage pain and lameness in dogs and some supplements can be incorporated into commercial diets, which may improve compliance of administration by owners.[9,18] While NSAIDs and other pain-directed treatments for OA will likely be necessary, reducing their use will improve long-term prognosis and quality of life for dogs.[19]

SPECIFIC DIETS AND SUPPLEMENTS

Calorie Restriction and Weight Loss

Slowing OA progression: Dietary (calorie) restriction to maintain body weight to optimal body condition score (BCS) has been found to have a significant effect on OA development over the life span of dogs.[13,20] Articular cartilage loss in appendicular joints in dogs and humans has been associated with the long-term stress exerted on joints by excess body weight.[21, 22]

Lifetime dietary restriction of caloric intake to maintain a lean BCS in dogs results in reduced radiographic evidence of OA in multiple joints, including reduced presence of OA in the hips and shoulders.[13,22-24] Radiographic progression of elbow OA is slowed in dogs by lifetime caloric restriction as seen by reduced severity scores at 6 years of age; however, prevalence of elbow OA—in Labrador Retrievers, at least—is unaffected by reduced caloric intake.[25] In the elbow, high BCS may predispose to development of OA and for both the elbow and hip, diets high in fat and with an increased proportion of energy from fat may contribute to OA prevalence.[26] Maintaining BCS < 6 out of 9 has significant effects on development of OA during growth and the prevalence of OA over the entire lifespan of large or giant breed dogs.[13,22] Excessive stress on joints from increased body weight results in articular cartilage loss, lameness, and pain.[21,27-29] Reduction of body weight by approximately 6–8% in overweight dogs with OA results in reduced lameness and improvement in owner perception of weight-bearing.[27] Combined with rehabilitation, caloric restriction improves function in dogs, indicating that improving mobility in overweight dogs with OA may be best accomplished by both weight reduction and rehabilitation.[30] Weight reduction of 10% in humans reduces articular cartilage loss but even 5% reduces OA progression in a 4-year period.[31] Further guidelines can be found in the chapter on Overweight and Obesity in Dogs and Cats.

Pain/lameness: The combination of reduced caloric intake (by 25% in puppies predisposed to developmental orthopedic disease and OA) and body weight reduction (to a BCS 4–5/9 if overweight as an adult) will improve objective kinetic gait measurements such as peak vertical force and vertical impulse as well as improve subjective owner assessments of lameness and quality of life.[23,24,27,31,32]

COMMUNICATION TIP

"Many emerging supplements and nutritional strategies are available for OA; however, further investigation of their efficacy and effects is needed."

Protein

Slowing OA progression: Another essential nutrient is protein, and it is important for dogs with OA because while lower body mass reduces stress on joints, greater muscle mass in individuals with OA results in slower progression of joint degeneration.[30,33] Increased protein in the diet can improve response to rehabilitation by providing amino acids for muscle mass development.[34,35] Increased protein additionally improves satiety, which may improve owner compliance on a calorie-restricted diet.[36] A therapeutic diet with 9 g protein/100 kcal or 30% protein on dry matter basis (DMB) and omega-3 fatty acids slowed OA progression and improved recovery in dogs following cranial cruciate ligament surgery (CCLS), and the diet's effects were enhanced when physiotherapy was included.[34,37]

Pain/lameness: There is no research on the effect of dietary protein on pain and lameness in dogs with OA.

Omega-3 Fatty Acids (n-3 Fatty Acids)

Slowing OA progression: Labrador Retrievers fed a fish-based diet with 2.21% n-3 fatty acids on an as fed basis, as well as nutraceuticals for joint health, from 3 to 12 months of age had reduced severity of OA progression compared with littermates fed a chicken-based control diet without the nutraceuticals.[38] An

n-3 fatty acid-supplemented diet fed following CCLS resulted in improved weight-bearing on objective kinetic gait analysis, reduced owner reported lameness, and reduced radiographic OA progression in the 6 months following surgery.[34,37] Omega-3 fatty acids are most efficacious in reducing catabolic enzymes such as matrix metalloproteinases and serum inflammatory biomarkers including arachidonic acid, which may explain their effects on OA.[36,39-42] Diets specifically formulated with n-3 fatty acids reduce OA progression and improve weight-bearing in dogs and provide an easily administered method for owners to manage their dogs.

Pain/lameness: Numerous studies support the use of these anticatabolic supplements for objective and subjective pain relief and reduction in lameness in dogs as well as improved quality of life.[9,10,37,41,43-46] Competition for enzymes by omega-6 fatty acids may affect the response of dogs to omega-3 fatty acids; therefore, their relative intake by dogs must be monitored, or owners may feed a diet formulated with high n-3 fatty acid content.[47]

Hyaluronic Acid

Slowing OA progression: Hyaluronic acid (HA) is a glycosaminoglycan synthesized by chondrocytes and synovial cells and is a component of joint fluid and articular cartilage providing the joint with lubrication and shock absorption.[48,49] In OA, intraarticular HA is reduced, and oral administration of HA does result in its deposition in joint tissues in dogs.[50] Supplementation (1 mg/kg/day) to dogs following CCLS resulted in increased synovial HA concentration and reduced OA biomarkers.[48] Oral HA (1 mg/kg/day) and collagen supplemented to Labrador Retriever puppies beginning at 3 months of age reduced the prevalence and severity of elbow dysplasia and OA until at least 20 months of age.[51]

Pain/lameness: HA supplementation to working dogs with OA did not improve subjective assessments of lameness compared with carprofen and did not improve weight-bearing following CCLS;[52] however, HA administered as a preventative in growing Labrador puppies, along with other supplements, reduced lameness compared with controls.[51]

Green-Lipped Mussel (*Perna Canaliculus*, GLM)

Slowing OA progression: Extract from GLM has been shown experimentally to reduce cartilage loss and slow OA progression; however, omega-3 fatty acids from fish oil may be more effective in sparing cartilage damage than GLM.[53,54] A stabilized lipid extract has improved the response of individuals with OA.[18]

Pain/lameness: In subjective assessments by owners and veterinarians blinded to treatment versus placebo, dogs fed 0.3% (DMB) GLM in the diet or 20–49 mg/kg body weight/day supplementation had reduced joint swelling, lameness, and pain.[55,56] Doses of 11 mg/kg/day failed to show any difference to placebo; however, doses > 20 mg/kg/day improved activity and weight-bearing on objective gait analysis.[57-61]

Glucosamine and Chondroitin Sulfate (GCS)

Slowing OA progression: GCS has been studied extensively and is a component of articular cartilage and other joint structures.[62,63] The bioavailability of these functional ingredients can be poor, making their formulations more important for studies of efficacy and disease progression modification.[4] Improvements in formulations and dosage recommendations have indicated that GCS (15–30 mg/kg/day) slows cartilage degradation and OA progression when used long-term.[60,63,64] As components of non-arthritic joints, these molecules become reduced in an OA-affected state and supplementation signals chondrocytes to respond to cell signaling in a non-arthritic way.[18,41,65,66]

Pain/lameness: The ability of GCS to inhibit OA-mediated pain has been found to be poor.[42]

CONCLUSION

Many emerging supplements and nutritional strategies are available for OA; however, further investigation of their efficacy and effects is needed. There are additional supplements that have not been discussed in this chapter. Different formulations of nutraceuticals will have different bioavailability, and this must be considered when recommending these supplements. As little as 50% of products on the market today meet their label claims.[67] The bioavailability of some supplements may be enhanced during the extraction and preparation process, or rapid oxidation may limit their shelf-life.

Table 1. Nutritional intervention and its effects on dogs with OA
DMB, dry matter basis; FAs, fatty acids; EPA, eicosapentaenoic acid; DHA, docosahexaenoic acid; TPLO, tibial plateau leveling osteotomy

Nutritional intervention	Dose	Evidence-based effect on OA progression	Evidence-based effect on OA clinical signs	References
Dietary caloric restriction over lifespan	Maintenance of BCS 4-5/9	Reduced prevalence in hip and shoulder Reduced severity elbow and hip	Improved objective kinetic gait Reduced lameness on subjective assessments in hip and shoulder	23,24
Weight loss	0.5-2% body weight loss per week	Reduced inflammation and cartilage degradation	Improved objective kinetic gait Reduced lameness on subjective owner assessments	27,31,32
Dietary protein	30% DMB or > 9 g/100 kcal	Increased lean muscle mass, improved joint stability Reduced radiographic OA progression combined with omega-3 enhanced diet within 6 months following TPLO	Improved objective kinetic gait Reduced lameness on subjective owner assessments	30,34,35,37
Omega-3 fatty acids	2-2.9% EPA-DHA DMB 3.5% Omega-3 FAs DMB EPA+ DHA between 100 and 300 mg/(kg of body weight)$^{0.75}$ per day	Reduced radiographic OA progression within 6 months following TPLO Reduced radiographic OA severity at 12 months of age in hip and elbow Reduced joint catabolic enzymes	Improved objective kinetic gait Reduced lameness on subjective owner assessments	10,19,34,38, 42-46, 53,68,69
Green-lipped mussel (*Perna canaliculus*)	20-49 mg/kg body weight/day 0.3% DMB in diet	Reduced experimental cartilage damage and loss	Reduced subjective joint pain, swelling Objective kinetic gait analysis increased weight bearing over placebo but less than carprofen	53-57
Glucosamine & chondroitin sulfate	15-30 mg/kg body weight chondroitin sulfate	Reduced radiographic OA progression	No benefit on clinical signs	18,41,65,66
Hyaluronic acid	1.0 mg/kg body weight/day	Increased synovial fluid HA and reduced OA biomarker Reduced prevalence and severity in elbow dysplasia	Reduced lameness on subjective assessments	48,51,52

Table 2. Nutritional recommendations

	Diet	Potential supplements	Additional considerations
Growing puppy of breed at risk of developmental orthopedic disease and OA	Dietary restriction to maintain BCS 4–5/9 with diet 3.5–4.0 kcal/g Calcium to phosphorus ratio 1.1 to 1.2:1 for large breeds[14] Limitation of fat content[70]	Omega-3 fatty acids (total EPA and DHA minimum 100 mg/kg body weight/day) Hyaluronic acid Glucosamine & chondroitin sulfate	Formulated diets for large-giant breed puppies contain most supplements and restrictions, assess label amounts
Young adult at risk of OA	Dietary restriction or weight loss for maintenance of ideal BCS ≤ 6	Omega-3 fatty acids (total EPA and DHA minimum 100 mg/kg/day) Hyaluronic acid Glucosamine & chondroitin sulfate or green-lipped mussel Other supplements may also be available	Moderate intensity exercise and focus on lean muscle development to reduce risk of OA Other strategies such as disease-modifying drugs may be needed
Adult with mild/ moderate OA	Weight loss if BCS > 6/9 Fish-based diet or supplementation with omega-3 fatty acids	Omega-3 fatty acids (total EPA and DHA minimum 100 mg/kg/day) Hyaluronic acid	Multimodal therapy of OA required Not all supplements administered simultaneously, rather reserve some for OA progression Add analgesics such as monoclonal antibody to nerve growth factor,[71] amitriptyline, amantadine, gabapentin, etc.[69]
Adult with severe OA	Weight loss if BCS > 6/9 Dietary protein > 9 g/100 kcal	Omega-3 fatty acids (total EPA and DHA minimum 100 mg/kg/day)	Multimodal therapy of OA Improve muscle mass and activity Intermittent NSAIDs administered as needed Add analgesics such as monoclonal antibody to nerve growth factor, amitriptyline, amantadine, gabapentin, etc.
Geriatric with OA	Weight loss if BCS > 6/9 Dietary protein > 9 g/100 kcal (sarcopenia risk)	Omega-3 fatty acids (total EPA and DHA minimum 100 mg/kg/day)	Consider comorbidities when devising therapy Add analgesics such as monoclonal antibody to nerve growth factor, amitriptyline, amantadine, gabapentin, etc.

To date, the largest body of evidence supports weight management and dietary supplementation with omega-3 fatty acids for management of OA. While further developments on different supplements and dietary strategies for the prevention and management of OA are on the way, understanding the rationale behind each nutritional method will help practitioners tailor their multimodal protocol to each individual dog. Pet owners may become overwhelmed by the large number of supplements marketed for joint health, and veterinary teams are encouraged to use an evidence-based approach to guide the selection of nutritional interventions for their patients.

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DEGENERATIVE JOINT DISEASE IN CATS

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KEY TAKEAWAYS

- Feline DJD is very common in older cats, but often not recognized as such by veterinarians and pet owners.
- Feline DJD diagnosis should be based on history, clinical signs, orthopedic exam, and radiographs.
- Management of feline DJD should be multimodal: current evidence suggests a combination of drug therapy, environmental changes, weight management, dietary modification (or supplements), and therapeutic exercise (e.g., rehabilitation) may be the best approach.

DEFINITION

Feline degenerative joint disease (DJD) is a common, worldwide disease affecting domestic cats, with unknown etiology. Research on feline DJD is limited, and therefore most recommendations are based on findings in other species.

EPIDEMIOLOGY

An epidemiological study evaluating the radiological presence of feline DJD in 100 cats over 6 years of age revealed an overall prevalence of 61%, and prevalence increased with age.[1] A more recent study revealed similar results with an overall prevalence of 74% in cats that were screened for osteoarthritis on request of the owners.[2] In screening studies, most affected joints in cats with DJD were reported to be shoulders, elbows, hips, tarsal joints, and the intervertebral joints.[1,2]

RISK FACTORS FOR DEVELOPMENT OF FELINE DEGENERATIVE JOINT DISEASE

Feline DJD is more often seen in older cats, although cases have been reported from a wide range of ages.[2-5] No specific breed predisposition has been identified, but several studies have found a higher proportion of domestic short-hair cats affected.[2] Furthermore, being overweight or obese is considered a risk factor for feline DJD, similar to dogs and people.[6] Feline DJD can be secondary due to developmental orthopedic disorders (e.g., hip dysplasia), trauma, excessive vitamin A intake, joint surgery, or other forms of arthritis.

PATHOGENESIS

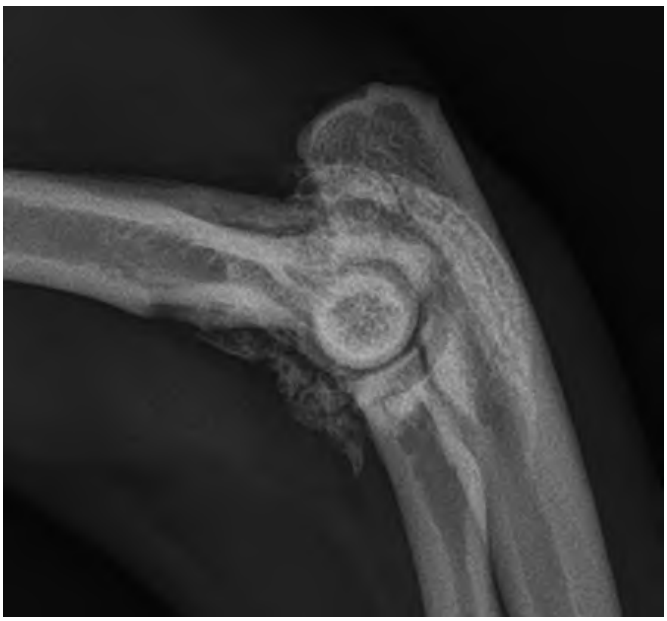
Normal joint cartilage is composed of collagen, proteoglycans, and water, and is designed to withstand forces during normal movement to prevent damage to the subchondral bone due to the unique balance among these components. During normal movement there is an interchange of nutrients and waste products between cartilage and synovial fluid, resulting in a balance between anabolic and catabolic factors within the joint. When these balances are disturbed due to trauma, age-related changes to the cartilage, or inflammation, a self-perpetuating cycle of cartilage degeneration is initiated, resulting in joint dysfunction and chronic pain. These processes result in repair cartilage of a lower quality compared with the original cartilage, chronic inflammation of the joint tissues, change of synovial fluid composition, formation of bone spurs, and sclerosis of the subchondral bone.

CLINICAL APPROACH TO INVESTIGATION

Clinical signs in cats are more subtle than in dogs, as cats often do not demonstrate overt lameness.[7] Instead, they show signs that are typically associated with older cats, some of which are in fact signs that are quite specific for DJD (although some of these signs can also be associated with other diseases that induce lethargy and/or muscle weakness, so they warrant further

investigation). These signs include grumpiness, less grooming behavior, less interaction with the owner and/or other pets, reduced ability to jump, and not getting onto higher spots within the household anymore.[8] The use of standardized owner questionnaires may be helpful as diagnostic tools.[1] The feline musculoskeletal pain index (FMPI) is considered the most reliable questionnaire at the moment (https://cvm.ncsu.edu/research/labs/clinical-sciences/comparative-pain-research/clinical-metrology-instruments/).[9,10] Orthopedic examinations can be challenging in cats due to their small body size and resistance to restraint, which sometimes results in resentment.[11] Cats often respond adversely to hyperextension of the joints even in normal joint conditions, so this finding should be interpreted cautiously. Part of the orthopedic exam is to provide possibilities for cats to jump.[12] When obvious other causes of feline DJD (i.e., Scottish Fold osteochondrodysplasia and mucopolysaccharidosis) are ruled out, osteoarthritis is most likely, of which the bony changes (if present) can be confirmed by taking radiographs (e.g., **Figure 1).** Radiographic findings do not always correlate with clinical signs.[13] Furthermore, objective outcome measures like force plate analysis are difficult to perform in a clinical setting, and accelerometers only give an impression of the number of movements but not how these movements are performed.[14] Therefore, although subjective owner questionnaires are not necessarily the most reliable tools, they are often the only ones with some predictive value that can be used in private practice.

Figure 1. Radiograph from a cat with degenerative joint disease (courtesy of Dr. S. Veraa)



MANAGING FELINE DEGENERATIVE JOINT DISEASE

Management of feline DJD should be multimodal: current evidence suggests a combination of drug therapy, environmental changes, weight management, dietary modification (or supplements), and therapeutic exercise (e.g., physiotherapy) may be the best approach.

Drug Therapy

Meloxicam, robenacoxib, tramadol, and gabapentin have been shown to have efficacy in controlled studies in cats with DJD-related pain. Amitriptyline and amantadine are other potential therapies, although scientific evidence of efficacy is poor. Emerging therapies requiring future studies and safety data include anti-nerve growth factor antibody, piprants, cannabinoids, and mesenchymal stem cell therapy.[15]

Environmental Changes

Important environmental changes include improving access to higher places (e.g., sleeping areas); raising food bowls and water bowls to prevent the necessity of bending the neck; providing multiple feeding bowls, water bowls, and litter trays; adapting litter trays to make them easier to access and use; and providing warm beds.[12]

Weight Management

As being overweight or obese is considered a risk factor, weight management should be part of the treatment plan. Guidelines for designing and implementing a weight loss plan can be found elsewhere. This includes dietary management and exercise. Dietary management of overweight and osteoarthritis can be combined; however, when food intake is reduced, the intake of key nutrients and nutraceuticals might go below the recommended amounts, which should then be counteracted by adding supplements. Exercise will benefit both weight loss and preservation of lean body mass, as well as improve joint function.[16]

Dietary Management

Several functional ingredients may be beneficial to use in feline DJD patients; however, data on cats are scarce. These may be provided in the diet or as a supplement. **Table 1** lists common nutrients or functional ingredients and their suggested mechanism of action. Most evidence is available for the use of

omega-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) (dosage 120 mg/kg per day [ratio EPA:DHA 5:1]).[17] EPA and DHA are known for their anti-inflammatory effects, reducing osteoarthritis pain in several species, including cats. They also reduce the production of cartilage-degrading enzymes (matrix metalloproteinases [MMPs]).[18] For other nutraceuticals there is currently only limited evidence to support their use, but they are usually not harmful—these include glucosamine and chondroitin sulfate (225 mg and 175 mg, respectively, per cat, twice daily)[19] and a combination of green-lipped mussel, curcumin, and black currant leaf extract (120 mg, 50 mg, and 50 mg, respectively, daily).[20] A therapeutic diet enriched with EPA and DHA, green-lipped mussel extract, glucosamine, and chondroitin sulfate has also been shown to have efficacy.[21] Suggested mechanisms of action of glucosamine and chondroitin include functioning as building blocks of the cartilage glycosaminoglycan matrix and reducing the activity of cartilage-degrading MMPs. In green-lipped mussel, glucosamine and chondroitin are combined with eicosatetraenoic acid (ETA), which is a long-chain polyunsaturated omega-3 fatty acid and a precursor of EPA and DHA. Other components of green-lipped mussel are furan fatty acids (F-acids), sphingolipids, phytosterols, diacylglycerols, diterpenes, sesquiterpenes, and saponins, alongside antioxidants such as carotenoids, xanthophylls, and anthocyanins. Curcumin has anti-inflammatory properties. Black currant leaf extract contains several phytochemicals, such as proanthocyanidins, which dampen the inflammatory response and have a protective effect on cartilage of people with osteoarthritis.[20] A recent meta-analysis concluded that the use of omega-3 products beneficially modulates the painful condition of feline DJD, while the intake of chondroitin-glucosamine has no analgesic effect. Further studies will be necessary to be able to determine the potential effects and safety of collagen, cannabidiol, and composite functional ingredients, but these products seem promising (**Table 1**).[22]

COMMUNICATION TIP

Managing feline DJD often requires a combination of drug therapy, environmental changes, weight management, dietary modification or supplements, and therapeutic exercise.

Therapeutic Exercise

Rehabilitation can be helpful in feline DJD patients to maintain and improve the range of motion in joints and improve muscle strength and tone. Careful manipulation of joints as well as some forms of

Table 1. Functional ingredients for cats with degenerative joint disease ranked by current level of evidence

Functional ingredient	(Suggested) mechanism of action
Omega-3 fatty acids EPA and DHA	Anti-inflammatory
Type II collagen	Building blocks of matrix, anti-inflammatory, oral tolerance (undenatured)
Phytochemicals	Antioxidants
Glucosamine and chondroitin	Building blocks of matrix, anti-inflammatory
Cannabidiol	Analgesic (no studies in cats yet)

EPA = eicosapentaenoic acid, DHA = docosahexaenoic acid

therapeutic exercise are likely to effective. Some cats can also be encouraged to perform on an under-water treadmill and/or to swim.[23]

SUMMARY

Feline DJD often goes unrecognized by veterinarians and pet owners. Subjective owner questionnaires are often the only diagnostic tools with a certain level of predictability, but radiographs may help confirm the diagnosis. Management should be multimodal, consisting of a combination of drug therapy, environmental changes, weight management, dietary modification (or supplements), and therapeutic exercise (e.g., physiotherapy).

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PRACTICAL TOOL: ASSESSMENT OF CHRONIC PAIN IN DOGS AND CATS

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CHRONIC (MALADAPTIVE) PAIN

The features of chronic, or maladaptive pain, are well described in the 2022 WSAVA guidelines for the recognition, assessment and treatment of pain[1] and are listed in **Box 1.**

Box 1. Features of chronic (maladaptive) pain

- Persists beyond the expected course of the acute disease
- Not associated with healing
- Serves little to no biological purpose
- Can exist without a cause
- No clear endpoint
- Associated with recurrent or long-standing disease conditions, such as osteoarthritis

Chronic pain can be subdivided into 'neuropathic' and 'dysfunctional' pain. While neuropathic pain is initiated by a lesion within the peripheral or central nervous systems (e.g., nerve root compression, peripheral nerve sheath tumor), dysfunctional pain is where the peripheral nervous system is grossly normal but processing by the nervous system is abnormal.

ASSESSMENT OF CHRONIC PAIN IN CATS AND DOGS

In dogs and cats, chronic pain cannot be assessed directly, but only indirectly by assessment of pain behaviors. While objective measures of chronic pain behaviors are often used in a research setting (e.g., force platform to measure ground reaction forces in lameness), such techniques are not widely available in practice. In a clinical setting, validated questionnaires provide a time- and cost-effective alternative although the limitations of such tools must also be appreciated. Reasons to use tools to assess chronic pain are described in **Box 2.**

Validated questionnaires to assess chronic pain can be subdivided into those completed by veterinary professionals, and those completed by clients (client, or owner, reported outcomes measures; CROMs or OROMs). At the time of writing, CROMs for dogs and cats have generally received more validity testing than veterinary-undertaken tools. This may be a reflection of the insidious onset and subtle manifestation of chronic pain. Assessment of chronic pain behaviors requires time, observation during both day and night, and during a variety of activities. Consequently, it is owners that are best placed to provide information. The challenge for CROMs is to ask for that information in a clear and understandable format for the untrained caregiver.

To aid using CROMs in clinical practice, veterinarians should be able to translate the CROM score to clinical meaning by knowing the minimal clinically important difference (MCID) change. The MCID is defined as "the smallest difference in score in the domain of interest which clients perceive as beneficial." MCIDs for many veterinary CROMs have not yet been estimated, but data are emerging for some.[2]

ADOPTING TOOLS TO ASSESS CHRONIC PAIN IN VETERINARY PRACTICE

Veterinary professionals are accustomed to using acute pain scales in everyday practice, a positive change that has taken place over the last 25–30 years. Scales such as the short form of the Glasgow Composite Measure Pain Scale[3,4] and the Feline Grimace Scale[5,6] have become widely used and positively impact the welfare of dogs and cats in acute pain or undergoing surgical interventions. It is now time to develop such habits for chronic pain because there are many more dogs and cats suffering chronic pain than acute pain.

There are many advantages to using CROMs for chronic pain. Delivered well, they are time-efficient for clinics because they can be completed by clients ahead

Box 2. Reasons to consider use of CROM tools to assess chronic pain in dogs and cats

- Checklist tools can identify dogs and cats that may have chronic pain
- Client education: the tool helps educate clients on how chronic pain can affect their pet
- Client 'buy in': the client feels part of the pet healthcare team
- Time-efficient
- Cost-effective
- Improves clinical record keeping and communication between the veterinary care team
- Improves monitoring of dogs and cats with chronic pain
- Helps assess the impact of nutritional, medical, or surgical interventions
- Helps clients see impact of nutritional, medical, or surgical interventions

of a veterinary consultation or as a follow-up to an intervention. The questionnaires are informative for clients, directing them to consider the impact of chronic pain on their pet and, at the same time, educating clients as to the signs of chronic pain. Many clients will appreciate being involved in the assessment of their pet, and the use of CROMs should provide a higher quality of service to our clients and improve the welfare of their pets.

Veterinary technicians and nurses are key team members in using CROMs with clients and guiding them on how to complete these. There are various models whereby technicians and nurses can work with veterinarians as part of a multidisciplinary team.

LIMITATIONS OF TOOLS TO ASSESS CHRONIC PAIN IN VETERINARY PRACTICE

CROMs should always be used alongside professional veterinary input and assessment; the CROM output is informative but must be placed alongside other clinical information. In addition, when using a CROM following an intervention, the caregiver placebo effect must be considered.[7,8] That said, it has been shown that CROMs can distinguish between placebo and active treatment.[9]

TOOLS TO ASSESS CHRONIC PAIN IN CATS

Most work in cats has been performed around the recognition of chronic pain associated with degenerative joint disease (DJD). A tool, called the Feline Musculoskeletal Pain Screening Checklist, has been validated for the identification of cats with pain associated with DJD[10] (**Table 1**). This tool is highly recommended for use in cats because the progression of DJD may be so insidious and cats tend to 'hide' the impact of chronic pain with subtle changes in behavior that may go unnoticed by clients. The checklist can form the foundation of client education and undoubtedly owner education is essential to avoid chronic pain behaviors being passed off as normal aging.

There are also other tools to assess the severity of chronic pain associated with DJD in cats (Table 1). These CROMs have been designed to measure the impact of DJD pain on the cat and to assess the impact of interventions. Each instrument varies somewhat in what they measure but there is good agreement between them.[11] When administered repeatedly at intervals, these instruments can provide data on the severity of chronic DJD-associated pain and changes in impairment of mobility.

The 2022 WSAVA guidelines for the recognition, assessment and treatment of pain[1] recommend using the Feline Musculoskeletal Pain Screening Checklist for screening of patients at risk of DJD, and the FMPI or CSOM for monitoring signs of pain and response to treatment such as dietary modification.

TOOLS TO ASSESS CHRONIC PAIN IN DOGS

Development of CROMs for dogs has a longer history (**Table 2**). Chronic pain and mobility issues are easier for clients to detect in dogs because they tend to display pain behaviors more overtly, are exercised by clients, and are often keenly observed both at exercise and in the home. However, the fundamental principles of development and validation of CROMs are the same.

Because clients tend to self-report mobility issues in dogs, there has been more emphasis on tools to stage the severity of chronic pain or mobility issues.

Table 1. Tools for assessing chronic pain in cats

Tool	Type	Condition	Description/ comments	Link or source	References
Feline Musculoskeletal Pain Screening checklist *	Screening	DJD	Checklist of 6 activity items - if any item cannot be performed this should prompt further evaluation	https://cvm.ncsu.edu/research/labs/clinical-sciences/comparative-pain-research/clinical-metrology-instruments/	Enomoto et al, 2020[10]
Feline Musculoskeletal Pain Index (FMPI)*	CROM	DJD	Most validated feline CROM. FMPI-Short Form consists of 9 items related to mobility and daily activities	https://cvm.ncsu.edu/research/labs/clinical-sciences/comparative-pain-research/clinical-metrology-instruments/	Enomoto et al, 2021[12] Benito et al, 2013 and 2013a[13,14]
Client Specific Outcome Measure (CSOM)*	CROM	DJD	Not a standardized tool, but items are selected and tracked over time. Useful in a clinical setting but less robust for clinical studies and trials	https://cvm.ncsu.edu/research/labs/clinical-sciences/comparative-pain-research/clinical-metrology-instruments/	Lascelles et al, 2007[15]
Montreal Instrument for Cat Arthritis Testing for use by owners (MICAT(C))	CROM	DJD	Basic validation has been performed	Available as a supplementary material with the original reference	Klinck et al, 2018 and 2018a[16,17]
Feline Physical Function Formula (FPFF)	CROM	DJD	Basic validation has been performed	The items are described in the reference	Stadig et al, 2019[11]
Cat Health and Wellbeing (CHEW)	HRQOL	Any	Basic validation has been performed	Available as supplementary material with the original reference	Freeman et al, 2016[18]
Feline QOL measure	HRQOL	Any	Basic validation has been performed	The items are described in the reference	Tatlock et al, 2017[19]
VetMetrica HRQOL for cats	HRQOL	Any	Basic validation has been performed	https://www.newmetrica.com/vetmetrica-hrql/ (requires subscription)	Scott et al, 2021[20]

* Indicates the tool is recommended in 2022 WSAVA Guidelines for the recognition, assessment and treatment of pain[1]
CROM, client-reported outcomes measure; DJD, degenerative joint disease; HRQOL, health-related quality of life

Table 2. Tools for assessing chronic pain in dogs

Tool	Type	Condition	Description/ comments	Link or source	References
Canine Osteoarthritis Staging Tool (COAST)	Screening	OA	Preliminary validation performed Has three steps for grading the dog, the joint, and staging OA	https://www.galliprantvet.com/us/en/coast-tools	Cachon et al, 2018[21]
Bristol Osteoarthritis in Dogs	CROM	Cruciate disease	Superseded by Liverpool Osteoarthritis in Dogs (LOAD)*	Items illustrated in original article	Innes et al, 1998[22]
Canine Brief Pain Inventory (CBPI)*	CROM	OA and bone cancer	Validated	https://www.vet.upenn.edu/research/clinical-trials-vcic/our-services/pennchart/cbpi-tool	Ragetly et al, 2019[23] Brown et al, 2008, 2009, 2013 and 2013a[24-27]
Liverpool Osteoarthritis in Dogs (LOAD)*	CROM	OA	Validated Licensed exclusively by Elanco Animal Health Ltd. Free to use with permission from Elanco	https://www.galliprantvet.com/us/en/coast-tools	Innes et al, 2023[2] Radke et al, 2022[28] Alves et al, 2022[29] Walton et al, 2013[30]
Helsinki Chronic Pain Index (HCPI)	CROM	OA	Basic validation performed Exclusively available in an app	https://www.pawesomer.com/ (paid subscription)	Walton et al, 2013[30] Matsubara et al, 2019[31] Hielm-Bjorkman et al, 2009[32]
Hudson Texas A&M Index	CROM	Lameness	Basic validation reported	The items are described in the article	Hudson et al, 2004[33]
Subjective nighttime restlessness evaluation (SNORE)	CROM	Quality of night-time sleep in OA	Basic validation reported	https://cvm.ncsu.edu/research/labs/clinical-sciences/comparative-pain-research/clinical-metrology-instruments/	Knazovicky et al, 2015[34]
Health-related quality of life (HRQOL)	HRQOL	Chronic disease	Validated	https://www.newmetrica.com/vetmetrica-hrql/ (paid subscription)	Reid et al, 2013 and 2018[35,36]

* Indicates the tool is recommended in 2022 WSAVA Guidelines for the recognition, assessment and treatment of pain[1]
CROM, client-reported outcomes measure; OA, osteoarthritis; HRQOL, health-related quality of life

However, recently, attention has turned to screening and initial staging of osteoarthritis in dogs with the development of the Canine Osteoarthritis Staging Tool (COAST).[21] COAST combines a user-defined CROM with veterinarian-assessed scoring of joint pain.

There is significant choice of CROMs to assess chronic pain or mobility issues in dogs, but the COSMIN initiative (COnsensus-Based Standards for the selection of health Measurement Instruments - www.cosmin.nl) is an international initiative aiming to develop tools for selecting the most suitable instrument for any given situation.

A COSMIN-based systematic review of CROMs in canine mobility was recently published.[15] Of the six CROMs evaluated, the authors concluded that three [Liverpool Osteoarthritis in Dogs (LOAD), Canine Orthopedic Index (COI), and the Canine Brief Pain Inventory (CBPI)] provided sufficient validity and can be recommended for dogs with osteoarthritis. The CBPI and LOAD are also recommended for use by the WSAVA.[1]

SUMMARY

Multiple tools are now available to evaluate and monitor chronic pain and mobility issues in dogs and cats. When clinicians are using nutritional management and interventions for mobility issues in dogs and cats, as well as tracking traditional metrics such as bodyweight, it is highly recommended that a CROM is used to track the severity of chronic pain and its impact on mobility.

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LOWER URINARY TRACT DISORDERS

STRUVITE AND CALCIUM OXALATE UROLITHIASIS IN CATS

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KEY TAKEAWAYS

- Struvite and calcium oxalate uroliths together account for > 90% of all feline uroliths.
- Most feline struvite uroliths are sterile, and the treatment of choice is usually dietary dissolution as this has been shown to be highly effective.
- As uroliths can be recurrent in individuals predisposed, long-term prevention involves the use of diets designed to minimize the risks of both struvite and calcium oxalate urolith formation.

Urolithiasis is the macroscopic accumulation of crystalloid material (uroliths or "stones") in the urinary tract. This is distinct from crystalluria—microscopic crystals in the urine—which is a normal finding in many cats. A variety of urolith types occur in cats, but the most common are 'struvite' (composed primarily of magnesium, ammonium, and phosphate) and calcium oxalate (CaOx).

EPIDEMIOLOGY

Feline lower urinary tract disease accounts for ~2–5% of cases in primary care practice,[1–3] and typically 10–30% of these are caused by urolithiasis.[3–6] Worldwide, struvite and CaOx uroliths generally account for >90% of all feline uroliths.[3,7–16]

Studies from North America[14,17] show that in the early 1980s, CaOx uroliths were uncommon with struvite accounting for the vast majority of submissions for laboratory analysis. By the late 1990s the proportion of CaOx uroliths had markedly increased, and they accounted for well over 50% of all submissions. However, from the early 2000s the balance has shifted again, and currently struvite uroliths are a little more commonly identified than CaOx. Data from other regions of the world show similar trends, but with CaOx remaining predominant in most studies, albeit with some geographic variation.[3,8–11,13,15,16] Importantly, these studies do not provide a full picture, as they are only based on uroliths removed or voided and then submitted for analysis.

PATHOGENESIS AND RISK FACTORS

Urolithiasis has a complex, and often only partially understood pathophysiology. Crystal formation, growth, aggregation, and retention are all components of urolith development, and supersaturation of urine with calculogenic crystalloids is a fundamental requirement for this to occur. Many other factors are also important, including simple physical effects such as urination frequency and completeness of bladder emptying (which may affect voiding of crystals and early uroliths), lifestyle and dietary risks, the presence and balance of different urinary constituents that act as promoters and inhibitors of stone formation (including pH, other ions, citrate, and certain proteins and glycoproteins), sex, and genetics.[18–20]

The importance of factors in addition to crystalloid supersaturation is illustrated by studies showing that, depending in part on the diet, the prevalence of crystalluria in healthy cats is between 0% and 71% (typically 20–40%),[21–24] a prevalence vastly higher than that of urolithiasis. Freshly voided urine samples should be evaluated for crystalluria, as in vitro crystallization is common (especially with cooling of urine).[23,25] However, crystalluria without evidence of urolithiasis or urethral obstruction is not likely to require any intervention.

Epidemiological and other studies have identified a number of risk factors and predispositions for struvite and CaOx uroliths in cats, and some of these are shown in **Table 1.**[7–13,17–20,26–29] Risk factors do not necessarily imply causality, but some may be inter-related—for example, obesity, indoor lifestyle, and neutering might all be associated with increased food intake (including calculogenic minerals), with a more sedentary lifestyle, and with reduced frequency of urination.[8]

Table 1. Known and potential risk factors for development of struvite and CaOx uroliths[7-13,17-20,26-29]

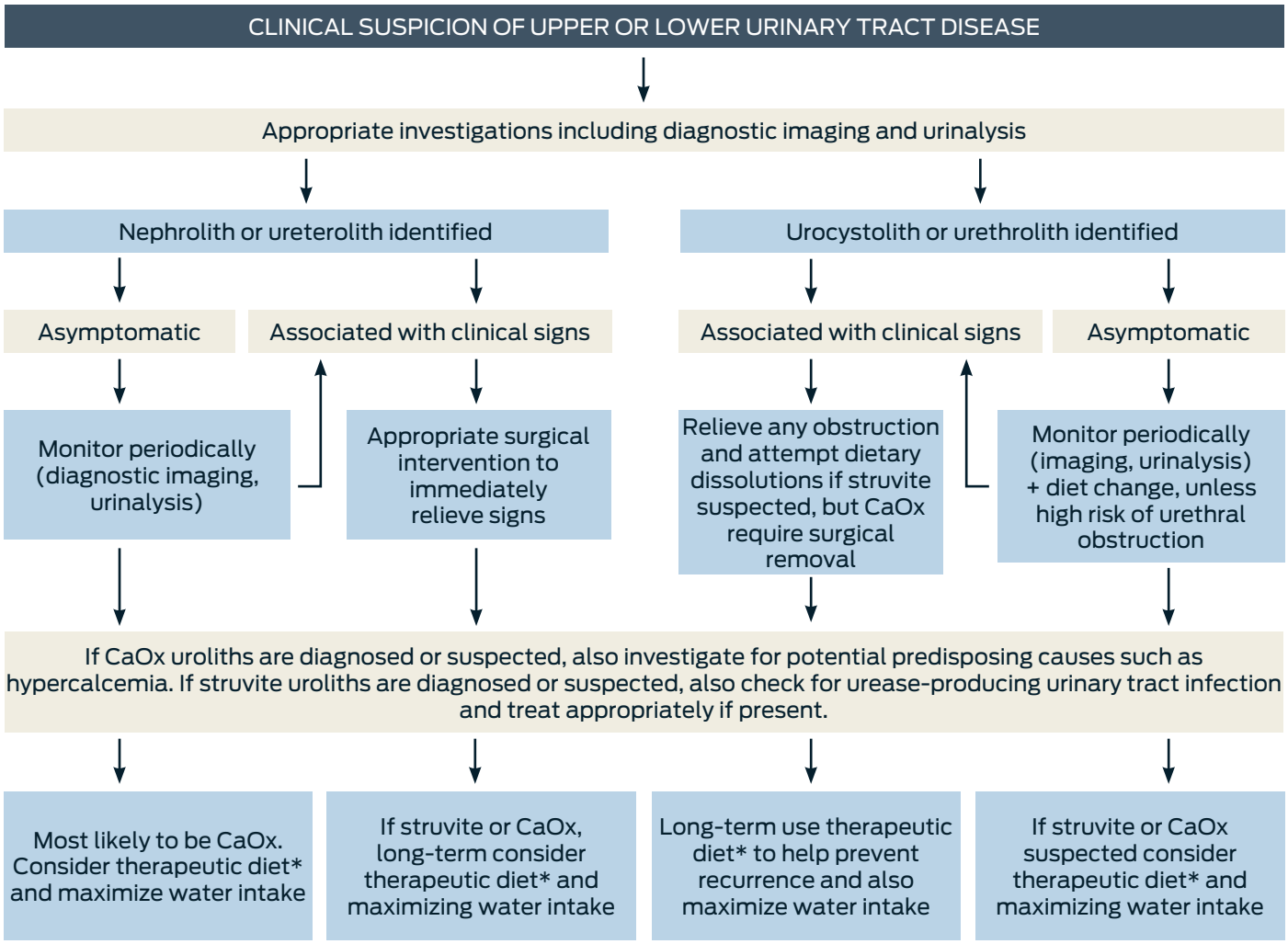
	Struvite uroliths	CaOx uroliths
Lifestyle	Obesity Indoor lifestyle	Obesity Indoor lifestyle Feeding highly acidifying diets
Breeds with increased risk (genetics)	Domestic shorthair Foreign shorthair Oriental shorthair Himalayan Ragdoll	Persian Himalayan Burmese British, Exotic, & Foreign shorthair, Siamese, Havana, Russian Blue, Ragdoll, Tonkinese, Devon Rex, Maine Coon, Domestic longhair
Sex	More common in females and in neutered cats	More common in males and in neutered cats
Age	Average: ~5–7 years old Typical range: 1–10 years old	Average age: ~6–8 years old Typical range: 4–15 years old
Urine composition	Concentrated urine More alkaline urine (typical pH ~7) Urease-producing urinary tract infections (but uncommon in cats where >90–95% are sterile)	Concentrated urine Highly acidic urine (typical pH < 6) Hypercalciuria
Metabolic factors		Hypercalcemia

DIETARY-RELATED RISK FACTORS

Diets high in phosphate and magnesium predispose to struvite uroliths.[30] Historically, dry diets high in magnesium were shown to induce struvite and other magnesium-containing uroliths,[14,29] but further studies identified a critical role for urine pH as acidification could prevent struvite formation even with a high magnesium diet.[29] It is hypothesized that the widespread use of modified commercial maintenance diets that were restricted in magnesium and designed to produce a highly acidic urine was responsible for the historical decline in the prevalence of struvite uroliths, and the concomitant increase in CaOx.[8,12,14,17,18] However, it is now known that moderately acidifying diets can be designed that minimize the risk of CaOx as well as struvite (see below). Whether genetic, metabolic, or other abnormalities underlie some cats naturally at risk of developing struvite uroliths remains unknown.

The development of CaOx uroliths is complex and poorly understood. Hypercalciuria is considered important[17–20] and may be due to underlying hypercalcemia in up to 35% of cases.[18–20,29] Epidemiologically, highly acidic urine is a risk factor for CaOx uroliths, which may be due to increased calciuria, reducing CaOx solubility and its effects on CaOx inhibitors.[30–32] Despite this, urine pH has a limited role in affecting CaOx saturation in experimental studies.[19,30,33,34] In humans, high protein diets increase the risk of CaOx uroliths, but although some studies are conflicting, the same does not appear to be true in cats, and higher protein diets may even be protective.[26,30–32,35–39] High levels of calcium in the diet may promote calciuria,[40] but this may depend in part on how it is supplemented.[41] Oxalate can be derived both from dietary sources and endogenous production (from some amino acids, sugars, and vitamin C),[30,31] but neither changes in macronutrients nor vitamin C supplementation appear to have an important effect on oxaluria in healthy cats.[32,42] Experimentally, pyridoxine (vitamin B6) deficiency causes hyperoxaluria, but adding B6 to a diet already replete has no further benefit.[18,30,31] Increased dietary sodium is another risk for CaOx uroliths in humans, but studies in cats suggest any increase in calciuria is more than outweighed by the increased urine volume with lower overall CaOx saturation.[35,40,43,44] Other factors that may increase

Figure 1. Flow chart giving a brief overview of CaOx and struvite urolith diagnosis and management



* A therapeutic veterinary diet can be chosen that is designed to meet all adult maintenance nutritional requirements and is additionally designed to undersaturate the urine or struvite (thus likely to achieve dissolution and prevention of struvite uroliths), and also achieve low metastable supersaturation dor CaOx to help prevent their recurrence. If treats are given or other elements are added to the diet, this may negatively impact its efficacy.

the risk of CaOx uroliths include reduced dietary magnesium, phosphate, and citrate (all of which inhibit CaOx crystallization).[17–19,29,31] However, importantly most studies of nutrition and urinary CaOx saturation have involved only small numbers of healthy cats, and not CaOx urolith-producing cats, which might have underlying metabolic abnormalities.

CLINICAL SIGNS

Most uroliths are found in the lower urinary tract (bladder and/or urethra).[10,13] Most are symptomatic, and typical signs include hematuria, dysuria, pollakiuria, periuria, and stranguria (if there is urethral obstruction).[32]

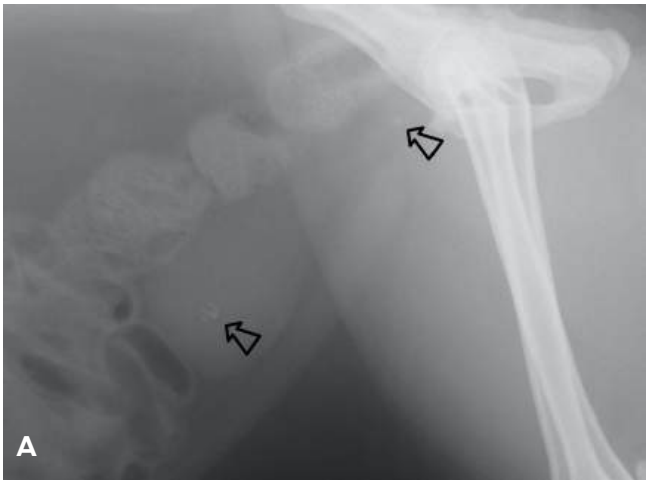
With the rise in prevalence of CaOx uroliths there has also been a marked increase in uroliths in the kidneys and ureters,[14] sites where >90% of uroliths are CaOx.[12,14,17,20,28,45] Detection of uroliths can be an incidental finding, especially with nephroliths.[45] If a nephrolith is causing obstruction, or is associated with pyelonephritis, pain may be present,[45] and most ureteroliths cause abdominal pain, hydronephrosis, vomiting, lethargy, hematuria, and/or signs of kidney disease.[46]

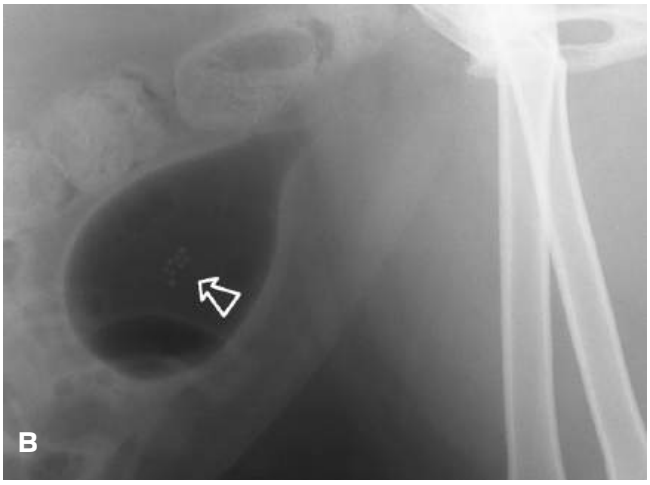
COMORBIDITIES

Important comorbidities include:

- Hypercalcemia (including idiopathic hypercalcemia) with CaOx uroliths.[18,19,29]

Figure 2. Plain abdominal radiograph (2A) and pneumocystogram (2B) of an 11yo neutered male domestic shorthair cat with multiple CaOx uroliths highlighted with arrows. Images courtesy of Dr. A. Sparkes





- Urease-producing urinary tract infections with struvite uroliths (although an uncommon association in cats).[20,29]
- Obstructive uropathy and acute kidney injury (AKI) with urethral obstruction.
- Chronic kidney disease (CKD) has been associated with kidney or ureteral uroliths,[27,47,48] although the uroliths may not accelerate the progression of CKD.[49]
- Nephroliths or ureteroliths causing ureteral obstruction may result in AKI.[17,45]

DIAGNOSIS

Diagnostic imaging (radiography, contrast radiography, ultrasonography, and CT) is the gold standard for diagnosis, and both struvite and CaOx uroliths are radiodense. Urine pH and the presence of crystalluria may help indicate the likely nature of a urolith, but results are variable, can be misleading, and crystalluria is not always present.[17,18,25,29] Urine specific gravity (USG) should be assessed along with urine culture to detect any concomitant urinary tract infection.[18] Serum biochemistry is also important to detect changes such as hypercalcemia.[17,18] Any uroliths that are voided or removed should ideally be analyzed quantitatively to accurately determine their nature.[18]

MANAGEMENT

Struvite uroliths can be dissolved medically, whereas CaOx cannot and require removal (where indicated).[17,18,30–32] There is a high risk of recurrence of uroliths,[40,44] so long-term medical management to reduce risks is indicated.[17,18,30–32] Consensus guidelines on managing uroliths have been published by the ACVIM,[50] and briefly these recommend:

- For suspected struvite uroliths, unless contra-indicated (e.g., urethral obstruction), medical dissolution should be attempted, which is highly effective.[50] Infected struvite uroliths require antimicrobial therapy to eliminate the infection.[18]
- Urocystoliths that cannot be dissolved and are not associated with clinical signs can be monitored (but should be removed if they are likely to obstruct the urethra).[50]
- Urethroliths should be managed by minimally invasive removal or retrograde hydropulsion followed by cystotomy.[50] Urethral surgery is discouraged, and urethrostomy should be avoided wherever possible.[50]
- Nephroliths not causing clinical signs should be monitored with radiographs and/or ultrasound, or attempt dissolution if struvite is suspected. With outflow obstruction, pain, recurrent infection, or compression of normal renal parenchyma, removal should be considered as most are CaOx.[50]
- Partial or complete ureteral obstruction should be treated as an emergency with appropriate intervention.[50]
- With CaOx uroliths, hypercalcemia should be identified, investigated, and treated appropriately.

Key Nutrients for Stone Management

Several commercially available therapeutic diets are designed to dissolve struvite uroliths and to help prevent recurrence of both struvite and CaOx.

Predicting the efficacy of dietary prevention can be problematic without large-scale and long-term studies in target populations, although a number of these diets have proven efficacy in dissolving naturally occurring struvite uroliths.[51–54]

COMMUNICATION TIP

Struvite and calcium oxalate stones can be associated with important comorbidities including hypercalcemia (CaOx), urinary tract infections (struvite, rare in cats), acute kidney injury, and chronic kidney disease.

Measuring the relative supersaturation (RSS) of the urolith-forming substance in urine (calculated from the pH and concentration of a range of solutes) helps predict the likely efficacy of a diet.[30,55] Low RSS values (absolute values depend on methodology) indicate urine is undersaturated and so dissolution can occur; moderate values indicate urine in the metastable supersaturated range where no spontaneous crystallization or dissolution will occur; and high values indicate urine in the labile supersaturated range where spontaneous crystallization may occur.[30]

Urine undersaturation (low RSS values) is achievable for struvite and will result in urolith dissolution as well as aiding prevention.[30,51–54] This is usually achieved through:[30–32,43,50]

- Avoiding excessive magnesium and phosphate in the diet.
- Producing a moderately acidic urine (e.g., ~pH 6.2–6.3).
- Ideally feeding a high moisture diet (>70–80%) to increase urine volume and reduce concentration; cats on dry food may benefit from a gradual transition to a wet diet.
- For cats that will not accept a wet food, a diet with moderately increased sodium (e.g., 300–350 mg/100 kcal) may be used to help increase water intake and reduce struvite concentration.
- Other strategies to increase water intake (see below) may also help to reduce urine concentration.
- Consuming several small meals during the day rather than one or two larger meals may also help minimize any post-prandial alkaluria.[30,31]
- Where uroliths are present, re-evaluation every 2–4 weeks has been recommended, and most dissolve within 30 days.[51–54] A lack of reduction in urolith size within 2–4 weeks may suggest they are non-struvite uroliths or are mixed/compound uroliths with other stone types present.[51–54]

Undersaturation of urine is not achievable for CaOx, so the aim is to achieve urine RSS in the low metastable region to help prevent recurrence.[30] This may be best achieved by:[30–32,43,50]

- Increasing water intake and the production of dilute urine (USG <1.025–1.030); this is considered the most beneficial intervention, and best achieved by feeding a high moisture (>70–80%) diet.
- Additional water consumption and urine dilution may be achieved by offering highly palatable viscous water-based products (e.g., 'nutrient-enriched water').[56–58]
- For cats that will not consume a moist diet, dry diets with moderately increased sodium (see above) may increase urine volume and lower CaOx RSS.[40,44]
- Avoiding high levels of dietary calcium may help reduce calciuria.
- As magnesium and phosphate may increase CaOx solubility, excessive restriction of these should be avoided.
- Where CaOx uroliths are still recurrent, additional urine dilution is indicated if possible, along with potentially the use of potassium citrate (150 mg/kg/day PO) as it may help inhibit CaOx formation, and/or hydrochlorothiazide (1 mg/kg PO q12h) as it decreases urinary CaOx saturation in healthy cats.[17,40,50,59]

As ideal nutritional goals to reducing risks of struvite and CaOx uroliths sometimes differ (e.g., urine pH, magnesium and phosphate concentrations), specific recommendations for therapeutic diets designed to address both types of uroliths are challenging. However, diets should be complete and balanced, meeting minimum NRC and AAFCO or FEDIAF requirements for

adult maintenance or the appropriate lifestage, and be designed to achieve an undersaturated RSS for struvite and a CaOx RSS in the lower metastable range.[30]

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FELINE IDIOPATHIC CYSTITIS

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KEY TAKEAWAYS

- FIC is a syndrome that affects mainly adult cats worldwide. It varies in severity and duration, with most affected cats having short episodes of disease with limited recurrence.
- FIC can only be diagnosed by excluding other potential causes of the clinical signs (i.e., dysuria, hematuria, pollakiuria, stranguria), and it is unknown if this is a single disease or a syndrome with multiple potential etiologies.
- Management of FIC is challenging, but current evidence suggests a combination of stress reduction, environmental enrichment, dietary modification, and increasing water intake may be the best approach.

Feline idiopathic cystitis (FIC) is a common disease of unknown etiology, affecting domestic cats worldwide. Despite numerous studies, our understanding of FIC remains poor, and knowledge of effective therapeutic interventions is limited.

EPIDEMIOLOGY OF FELINE LOWER URINARY TRACT DISEASE

Feline lower urinary tract disease (FLUTD) has been reported to account for around 2–5% of feline cases seen in primary care practice.[1-4] Clinical signs (typically involving one or more of pollakiuria, periuria, dysuria, hematuria, stranguria) are non-specific, and the most common identifiable causes include urolithiasis, bacterial cystitis, urethral plugs, urethral strictures, trauma, and neoplasia. When investigations (urinalysis, urine culture, and diagnostic imaging) fail to identify a specific underlying cause, FIC is a disease diagnosed by exclusion of other recognized causes of the signs. In most studies, FIC is the single most common diagnosis made in cats presenting with signs of FLUTD, and generally comprises around 55–65% of cases.[1,4-6]

RISK FACTORS FOR DEVELOPMENT OF FELINE IDIOPATHIC CYSTITIS

FIC is seen most commonly in young to middle-aged adult cats with a mean age of around 5–6 years old, although cases have been reported from a wide range of ages.[1,4,7,8] No specific breed predisposition has been identified. Several studies have found a higher proportion of male cats affected, and FIC may also be a common underlying cause of urethral obstruction in male cats, potentially including at least some cats with urethral plugs.[8-10] Further, the feeding of dry cat food has been suggested as a predisposing factor in some studies.[1,4]

Some case control studies have specifically looked at different risk factors for development of FIC. Obesity has been the most consistent risk factor identified in these studies. Other factors have been less consistently observed and vary between studies but have included potential stressors such as the cat being nervous, conflict with other cats, having less space, a lack of vantage points in the house, being in a multi-cat household, and less outdoor access.[1,4,6,7,11-13]

PATHOGENESIS OF FELINE IDIOPATHIC CYSTITIS

Whether FIC represents a single disease or a syndrome with multiple causes remains to be determined. Although many studies have investigated potential causes of FIC, these have often been conducted on limited numbers of cats, and sometimes on cats with severe persistent or recurrent disease that may not be typical of all cats with FIC.

A number of local bladder abnormalities have been identified in affected cats[1,8,9] including a compromised epithelial barrier, increased bladder wall permeability, and reduced concentrations of urinary glycosaminoglycans (GAGs), although it is unclear if

Figure 1. Cat with dysuria during an episode of FIC. Photograph courtesy of Dr. A. Sparkes

this finding is unique to FIC among cases of FLUTD. The compromised integrity of the bladder wall may contribute to inflammation of the bladder and leakage of serum proteins that may in turn contribute to urethral plug formation in male cats. Neurogenic inflammation may also be a part of the pathogenesis with evidence of sympathetic activation, increased C-fiber neuron sensitivity, and increased expression of substance P and substance P receptors. While attempts to find underlying infectious etiologies have been largely unrewarding, further studies are needed to investigate the potential role of viruses such as caliciviruses or feline morbillivirus.[14,15]

Along with bladder changes, systemic neurohormonal changes have also been found in cats with FIC. These have included small adrenal glands, and increased sympathetic stimulation but suppressed adrenocortical responses suggesting uncoupling of the sympathetic and hypothalamic-pituitary-adrenal axis in response to stress.[1,4,8] Epidemiological studies of risk factors also provide some evidence to support the common suggestion that FIC is related to stress, but the lack of consistency in identifying specific environmental stressors (e.g., multi-cat households, inter-cat conflict) as risk factors raises some questions. It has been proposed that early life experiences may be involved in modifying stress responses and predisposing to FIC, and perhaps to other stress-related disease manifestations including gastrointestinal, respiratory, dermatological, and behavioral signs.[1,4,8] However, further work is needed to investigate these hypotheses. Collectively, current data suggest that the pathogenesis of FIC is complex with both local bladder abnormalities and/or neurohormonal changes in at least a proportion of affected cats, with the potential at least that environmental stress may be involved in some. Current studies provide some intriguing insights, but we remain a long way from a unifying and proven concept of the pathogenesis of this complex disease.

CLINICAL APPROACH TO INVESTIGATION

FIC is diagnosed by excluding other recognized causes of FLUTD. Although FIC is the most common cause of signs of LUTD in cats, where clinical signs are persistent or recurrent other recognized causes of disease should be ruled out as far as possible, involving urinalysis (including sediment analysis and bacterial culture), and diagnostic imaging. These investigations will allow a specific diagnosis of most recognized causes of FLUTD, but bladder biopsy may also be required in some cases. If investigations fail to reveal a specific underlying cause, FIC is the presumed diagnosis.

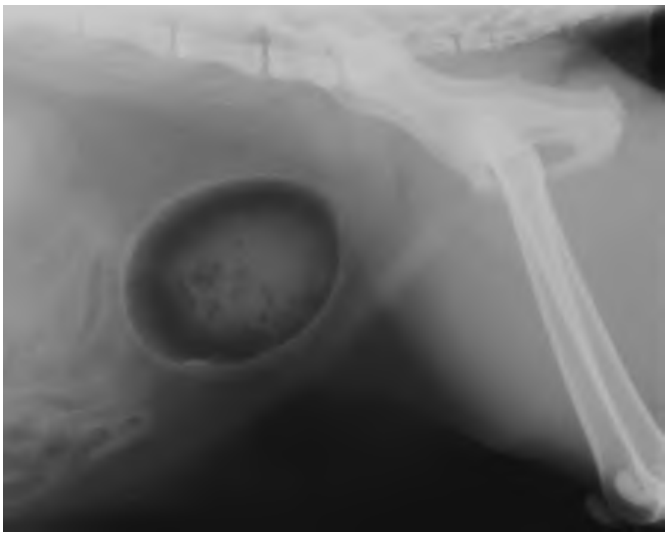
MANAGING FELINE IDIOPATHIC CYSTITIS

Because the etiopathogenesis of FIC remains poorly understood, management of the disease is challenging, and few interventions have any proven efficacy. Clinical signs in FIC often recur (with a variable frequency), but signs in each episode tend to spontaneously resolve within a few (typically 2–7) days.[1,16,17] This makes short-term assessment of therapy challenging and can lead to the false assumption that an intervention has had an effect rather than disease resolution being spontaneous. Further, as the frequency of recurrent episodes tends to reduce over time, this can complicate long-term studies of the disease

Drug Therapy

To date, no drugs (including prednisolone, anti-bacterials, meloxicam, propantheline, amitriptyline, and glycosaminoglycan replacers) have been demonstrated to be effective in controlled clinical trials of the management of FIC.[4,8,18,19] In one uncontrolled long-term study of cats with severe recurrent FIC, amitriptyline appeared potentially beneficial,[20] but further controlled studies are needed. Despite a lack of proven efficacy of pharmacotherapy in cats with FIC, the condition is assumed to be painful, and thus short-term analgesic therapy (e.g., with an opioid) is an important welfare consideration.[8]

Figure 2. Radiograph (double-contrast cystogram) of a cat with FIC showing a thickened bladder wall and blood clots causing lucency in the pool of contrast medium. Image courtesy of Dr. A. Sparkes / Animal Health Trust



Environment and Stress Management

Environmental management to reduce putative stressors is widely recommended for cats with FIC,[1,4,8] based partly on evidence that stress may play a role in the pathogenesis of the disease. Clinical observations and the results of an uncontrolled trial of cats with severe recurrent FIC[21] suggest that multi-modal environmental modification (MEMO) may be beneficial. Interestingly, there is evidence such environmental modification may also affect the severity of other co-morbidities in affected cats[21] but again, in the absence of good, controlled studies caution is still needed over any assumptions of the efficacy of such interventions.

An individualized approach to try to identify stressors (such as conflict between cats, lack of environmental interest or enrichment, lack of resting/hiding places) is important to try to identify specific potential causes of environmental stress. Good, effective communication with the owner is needed, and also to reassure them about the nature of the disease. The aim of MEMO is to create a more reassuring and safer environment for the cat, to reduce sources of stress, and through this to hopefully reduce pain levels, reduce the frequency of recurrent episodes, and improve the cat's welfare (**Box 1**).

Dietary Management

The only published controlled studies to date that have demonstrated a significant effect of an intervention in cats with FIC have been dietary trials.[22-24] Frustratingly though, it remains unclear what specific aspects of dietary intervention may be of benefit to these cats. In one non-randomized study, cats with FIC were followed over a 12-month period and fed either dry or canned versions of a therapeutic urinary diet.[23] Significantly fewer cats fed the wet diet had recurring clinical signs, and the urine specific gravity was significantly lower in the cats fed canned food (1.039 versus 1.051). These results have been widely interpreted to suggest an increased water intake and a reduced urine specific gravity are beneficial in cats with FIC, and along with MEMO this has become a standard recommendation.[1,4,18,19] At least one paper has recommended aiming for a urine specific gravity of <1.040 in affected cats.[18]

In two more recent studies,[22,24] including one that was a prospective randomized controlled study, the feeding of a therapeutic urinary diet was found to result in significantly fewer episodes of recurrent disease compared with a composite diet designed to mimic a typical supermarket diet,[22] or other commercial diets.[24] In one of the studies there was also tendency towards reduced recurrence in cats fed the wet form of the therapeutic diet.[24] Frustratingly, it is impossible to determine what aspects of the diet may have contributed to the improvement seen, but it would seem prudent to recommend the feeding of a high quality complete and balanced diet to cats with FIC where possible, and a therapeutic diet for lower urinary tract disease might have additional benefits. The latter may be particularly

COMMUNICATION TIP

Because the etiopathogenesis of FIC remains poorly understood, management of the disease is challenging. Clinical signs in FIC often recur (with a variable frequency), but signs in each episode tend to spontaneously resolve within a few days.

true for male cats affected by FIC where diets designed to reduce the risks of urolithiasis may also help to reduce the risk of urethral obstruction (where struvite crystals are a common component of a urethral plug). In addition to specific dietary modifications, if the cat is overweight, appropriate measures should be taken to reduce and normalize bodyweight.

Box 1. Overview of commonly recommended MEMO interventions[8, 21]

- Provide safe and appropriate places for all cats to hide and rest (including provision of vantage points)
- Provide opportunities to play (with toys and with people) and to engage in predatory behavior (e.g. toys, hiding food etc.)
- Make sure each cat in a multi-cat household can separate themselves (have multiple, separate resting and hiding places)
- Make sure each cat in a multi-cat household has separate access to key resources (food and water bowls, litter trays, scratching posts, toys, etc.)
- Ensure frequent and positive owner–cat social and play interactions
- Offer cats choices to express their preferences over resources, interaction, and play
- Avoid situations and circumstances that cause fear or anxiety for the cat
- Use appropriate synthetic environmental pheromone products

Some commercial diets incorporate nutrients that are purported to modify stress responses in cats (e.g., α-casozepine and/or l-tryptophan), or these can be administered as nutraceuticals; however, there is no published data to demonstrate the efficacy of these products in managing FIC.

Increasing Water Intake

While feeding wet rather than dry foods helps to increase water intake, increase the volume and frequency of urination, and reduce urine concentration, even when transitioned gradually not all cats adapt to a wet diet. The use of water fountains or water bowls with moving water has not been found to increase water intake in cats, although they may be preferred by some individuals,[25-27] whereas controlled studies have shown that dry urinary therapeutic diets with a moderately increased salt content (a sodium content of 300–350 mg/100 kcal) may successfully increase water intake and urine output,[18,19] as can the offering of a nutrient-enriched water source in addition to a water bowl.[28,29]

SUMMARY

Our current understanding of FIC remains relatively poor. Based on available published data and clinical experience, both of which may be flawed, the current emphasis in long-term management is on reducing stress through MEMO, increasing water intake and feeding a high-quality complete and balanced diet. Analgesic therapy in acute flare-ups of disease should be considered standard of care. Finally, in severe refractory cases there is some rationale in using long-term amitriptyline therapy, based on the results of a single uncontrolled study.

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PRACTICAL TOOL: USING IN-HOME TECHNOLOGY TO MONITOR FELINE LOWER URINARY TRACT HEALTH

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The term feline lower urinary tract signs (LUTS) is used to describe conditions affecting the bladder and/or urethra of cats. It is not a specific diagnosis and has been reported to occur in 4.5% to 8% of cats presenting to veterinary practices or teaching hospitals.[1,2] Inappropriate urination is one very common component of LUTS and is one of the most common reasons cats are relinquished to shelters.[3] Additionally, it is believed that there is a high percentage of the cat population that is not presented to veterinarians, and that cats are very good at masking, meaning they show little to no clinical signs in the early stages of disease. As a result, cats do not always receive treatment for health problems, including LUTS.

In addition to discussing a treatment plan for the underlying cause of LUTS and nutritional modification with owners, veterinary teams can be more proactive and recommend technology for the in-home setting (**Table 1**). In-home monitoring tools can be non-disruptive, allowing for reduced stress for the cat and owner and for earlier disease or recurrence detection. In-home monitoring tools may also signal a change associated with a health condition that requires a veterinarian's diagnosis and a veterinary visit. This is an advancement in health care where veterinary teams can provide earlier treatment and improve outcomes for cats and have more positive interactions with cat owners.

A complete urinalysis may require an appointment with the veterinarian, subjecting the cat to a stressful environment. In-home monitoring tools, including smart litterbox monitors, diagnostic cat litters, or litter additives can be excellent tools to assess a cat's urinary health in the home environment and can be a useful way to alert owners to a change in their cat's health. Diagnostic cat litter and litter additives monitor urine parameters only, such as hematuria. Smart litterbox monitors can assess urinary health through the collection of valuable data including body weight, frequency of litterbox use, and litterbox usage patterns. This allows an owner to monitor lower urinary tract health even when the cat is not observed while using the litterbox. The comprehensive data provided by some in-home monitoring tools give the pet owner and the veterinary team information about the cat's urinary and overall health.

Table 1. Examples of in-home monitoring tools for feline lower urinary tract signs. Cat owners can use these tools in their home and then alert their veterinary team and/or schedule a veterinary visit if any changes or abnormalities are detected.

Tool	Benefits
Smart litterbox monitors	Use artificial intelligence to learn an individual cat's unique litterbox patterns, allowing cat owners to identify subtle but meaningful changes in body weight, waste type, and elimination behavior
Diagnostic cat litter	Allows owners to monitor their cat's lower urinary tract health at home and helps avoid unnecessary vet visits and urine collection procedures; often can assess multiple health parameters with one product
Litter additives	Allow owners to monitor their cat's lower urinary tract health at home and help avoid unnecessary vet visits and urine collection procedures; often can only assess one health parameter

Monitoring tools that allow cat owners to track lower urinary tract health at home can also be helpful to owners and veterinarians who are following cats already diagnosed with chronic conditions including the major causes of LUTS – feline idiopathic cystitis and urolithiasis. It is important for veterinarians to be aware of validated in-home tests and connected devices that are available from quality manufacturers and to engage cat owners in novel ways to monitor their cat's urinary and overall health at home.

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STRUVITE AND CALCIUM OXALATE UROLITHIASIS IN DOGS

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KEY TAKEAWAYS

- Struvite stones are nearly always associated with urinary tract infections in dogs and diet is an adjunct to dissolution that typically is not required long-term.
- Diet can help reduce the rate and frequency of calcium oxalate stone formation.
- Lowering urine specific gravity through increasing moisture or sodium intake is helpful for urinary stone management.

PATHOPHYSIOLOGY AND RISK FACTORS

The formation of uroliths involves a complex interplay of crystalloid substrates, urinary pH, urine specific gravity, and the presence of crystallization promotors and inhibitors. Modification of diet and fluid intake can have substantial impact in the prevention and/or dissolution of urinary stones. A commonly used method for assessing the risk of calcium oxalate (CaOx) and struvite stone development in pet food manufacturing is relative supersaturation (RSS).[1] A solution that is supersaturated contains more solute than can be dissolved in the liquid, thus increasing the risk of stone formation. Determining the RSS of urine in a pet involves feeding a diet for a defined period of time (e.g., ≤ 2 weeks) and collecting urine over one to seven days. Along with urine pH, concentrations of crystal components and other ions such as calcium, magnesium, and phosphorus are recorded and entered into a software program for analysis and generation of RSS values.[2] While RSS can provide information regarding the stone risk of a particular diet, there are many other factors influencing the development of CaOx and struvite stones in dogs.

Calcium Oxalate Stones

Calcium oxalate stones make up approximately 47% of bladder stones in dogs.[3] The risk of developing CaOx uroliths is highest in middle-aged, neutered male dogs.[3,4] Breeds predisposed to developing this stone type include Miniature Schnauzer, Bichon Frise, Cairn Terrier, Chihuahua, Standard Poodle, Pomeranian, Japanese Chin, Brussels Griffon, Jack Russell Terrier, Miniature Pinscher, Lhasa Apso, Yorkshire Terrier, and Maltese.[3,4] Recurrence of CaOx stones is common, but the interval between stone formation can vary greatly by diet and breed. However, 59% of CaOx stone-forming dogs fed a maintenance diet had a stone recur within approximately 2 years, on average.[5]

Struvite Stones

Struvite stones are comprised of magnesium, ammonium, and phosphate. They are common bladder stones of dogs and represent about 44% of stones analyzed.[3] In contrast to CaOx, struvite stones are more common in young female dogs.[3] This difference is explained by the fact that struvite stones nearly always occur in the presence of urinary tract infections (UTI) with urease-producing organisms (typically *Staphylococcus* spp.) in dogs.[6] This is in contrast to cats that typically form sterile struvite bladder stones.

ROLE OF DIET IN TREATMENT AND PREVENTION

While diet plays a key role in the management of both CaOx and struvite bladder stones in dogs, the goals and temporal uses differ. Calcium oxalate stones cannot be dissolved and dietary management is aimed toward stone prevention (**Figure 1**). Struvite stones can be dissolved with a specialized diet and antimicrobial therapy, but long-term dietary therapy is not typically indicated (**Figure 2**). While the rationale for dietary modification differs for struvite and CaOx stones, diet plays an important role for both. In one study evaluating dogs with a history of CaOx stones, the rate

of recurrence was reduced by over half in dogs fed a stone-prevention diet (24% versus 59%). The length of time between stone formation was also over twice as long in dogs fed the preventative diet (5.6 versus 2.1 years).[5]

Diet is an effective adjunct to antimicrobial therapy in dogs with struvite stones.[7] Based on recent studies, a stone comprised of only struvite has a mean dissolution time of 31–35 days when treated with both diet and antimicrobials.[7,8] Stones that do not dissolve within a couple of months, despite appropriate medical therapy, are more likely to be a mixed stone or CaOx, although some struvite stones may take up to 4 months to dissolve.[7,8] Once an infection-induced struvite stone is dissolved, prevention should focus on managing future urinary tract infection. Foods designed or marketed to manage struvite urolithiasis will not prevent their recurrence in the face of a urease-producing UTI. However, these diets could potentially delay or reduce urolith formation in the presence of an undiagnosed UTI.[9] In rare instances where a dog has a sterile struvite stone, a long-term stone preventative diet is indicated.[10]

KEY NUTRIENT MODIFICATIONS

Water and Sodium for Diuresis

Maintaining a dilute urine is helpful for the prevention of all urinary bladder stones. More frequent urination can flush stone precursors and pathogenic bacteria from the bladder. It is also more difficult to reach supersaturation levels of solutes in dilute urine. There are several dietary strategies that can be used to reduce urine concentration. The first is to feed a high moisture diet. Diets with > 70% moisture can reduce urine specific gravity (USG) and CaOx RSS, though some breed differences may exist.[11] Most canned and home-prepared diets contain this level of moisture while dry kibble is generally less than 10% moisture.

The second dietary strategy aimed at promoting diuresis utilizes increased sodium content to promote thirst and water intake. Studies in dogs have demonstrated increased water intake, urine volume, and lower USG when feeding a dry commercial diet containing more than 250 mg sodium/100 kcal.[1,11-14] Given the detrimental effects of high sodium diets in people, the use of increased dietary sodium for the management of urolithiasis in dogs raises concern for some. While studies are sparse, to date there has been no documented effect of high dietary sodium on renal function, cardiac function, or blood pressure in dogs.[15-17]

COMMUNICATION TIP

"While a urinary diet is fed, treats should be limited to less than 10% of calorie intake. Ideally, any treats should be labeled as having RSS values compatible with stone prevention."

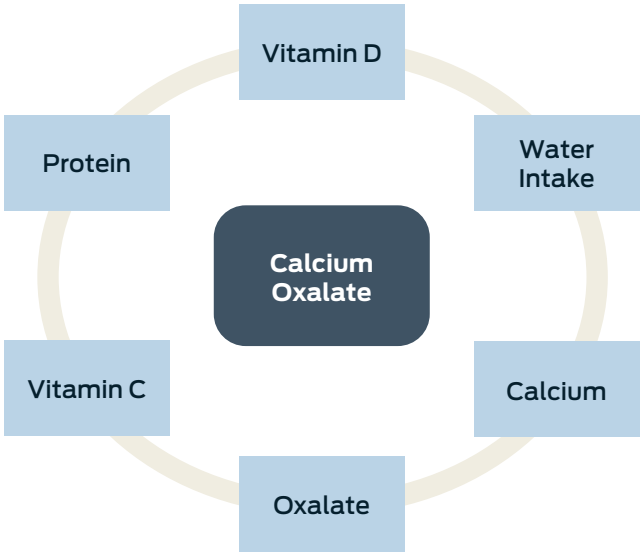
In people, increasing sodium intake increases calcium excretion in the urine.[18] This effect has also been demonstrated in dogs.[12,14] Despite the increased excretion, the high sodium diets can nearly double urine volume and lower concentrations of struvite and CaOx stone precursors and RSS values.[12,14] Thus, the increased urinary excretion of calcium due to high sodium intake seems less impactful compared with the positive effects on urine output. Studies evaluating the bone mineral density of dogs consuming a high sodium diet long-term are lacking and would be valuable to further assess the safety of high salt diets in dogs.

Protein

Diets high in animal protein and sulfur-containing amino acids can result in a metabolic acidosis and hypercalciuria in people, thus potentially increasing the risk of CaOx stone formation.[19,20] In dogs, high dietary protein may actually be protective against CaOx stone formation, although more research is needed to clarify this effect.[21,22]

The impact of dietary protein on struvite stone dissolution in dogs with infection-induced stones is unclear. Some struvite dissolution diets utilize very low protein levels to reduce stone precursors such as urea, ammonium, and phosphorus and promote a low urine specific gravity through medullary washout in the kidneys. While this dietary strategy is effective, struvite stones can also be dissolved using a moderate to high protein content and appropriate antimicrobial therapy is likely more important than dietary protein.[8]

Figure 1. Dietary factors contributing to calcium oxalate stone formation



The recurrence of calcium oxalate stones can be reduced by feeding high moisture diets with moderate, but not restricted, levels of calcium and avoiding high oxalate ingredients. High dietary protein and supplementation with vitamins C and D should also be avoided.

pH

Metabolic acidosis can lead to hypercalciuria as calcium is released from bone during the buffering process. Very acidic urine has been shown to promote CaOx crystallization and adhesion in canine kidney cells and increases the odds of CaOx stone formation in dogs.[23,24] Therefore, diets that promote formation of very acidic urine should be avoided.[9]

The formation of struvite stones is facilitated by alkaline pH which causes phosphate ions to reside in a trivalent state that more readily forms crystals.[1] Targeting slightly acidic urine pH (< 6.5) may be helpful to speed medical dissolution of infection-induced struvite stones, but more data is needed to determine the clinical impact of urinary acidification in dogs.

PRECURSORS AND INHIBITORS

Calcium Oxalate

Oxalic acid is a compound found in many food ingredients with highest concentrations in certain vegetables, legumes, and grains. It can also be formed endogenously and creates an insoluble salt with calcium ions. In humans, high dietary oxalate intake increases the risk of CaOx stone formation, but this impact is influenced by the concentration of oxalate consumed, the amount of dietary calcium (calcium binds oxalate and reduces intestinal absorption), and the presence of intestinal bacteria that degrade oxalate.[25] Despite the importance of high urinary oxalate on stone formation in humans, dogs with CaOx stones appear to have similar urinary oxalate concentrations as healthy dogs.[26]

Increased urinary calcium is a risk factor for CaOx stone formation in dogs. Hypercalciuria may result from hypercalcemia (e.g., hyperparathyroidism), increased intestinal absorption of calcium, bone resorption, or impaired renal reabsorption of calcium.[27] Administration of glucocorticoids, loop diuretics, urinary acidifiers, and vitamins D and C may also increase the calcium content of urine.[27] Although reducing urinary calcium concentration is key to CaOx stone prevention, dietary calcium should be maintained at a moderate level. Restricting calcium below recommended levels increases the risk of hyperparathyroidism and bone resorption, thus increasing urinary calcium. Dietary calcium also binds oxalic acid in the intestines, which reduces absorption of both stone precursors.

Struvite

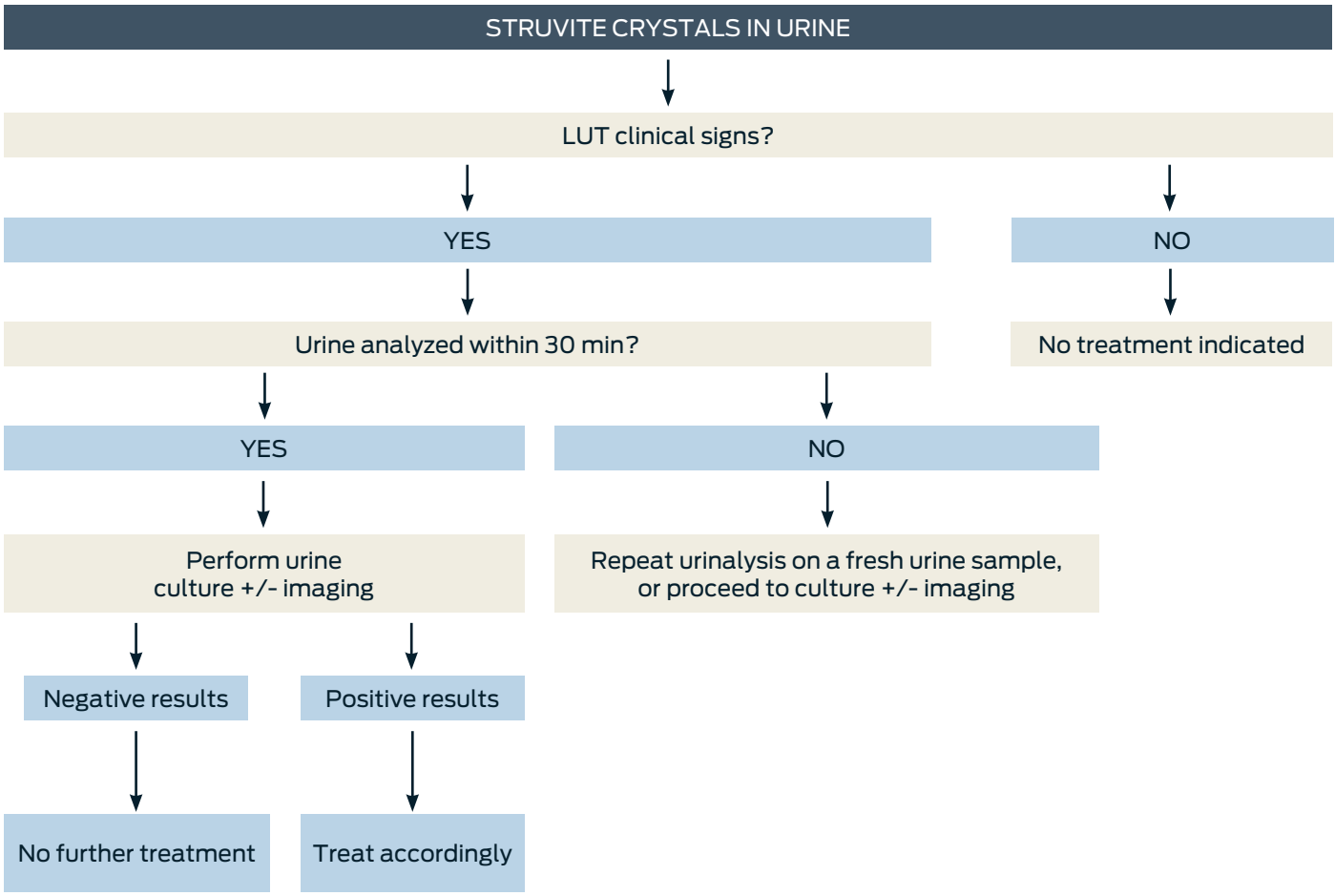
The formation of struvite stones requires oversaturation of magnesium, ammonium, and phosphate ions and high dietary levels of these ions increase their urinary excretion. However, based on data in cats, urine dilution and pH appear to be more important dietary factors for lowering struvite RSS than limiting dietary concentrations of stone precursors.[1] Dietary magnesium, phosphorus, and protein should be provided at adequate, but not restricted, amounts to reduce urinary concentrations of the precursors while meeting nutritional needs.

DIET OPTIONS

Calcium Oxalate

Because calcium oxalate stones cannot be dissolved, dietary management is focused on prevention. Choosing a high moisture diet with moderate levels of calcium and low-oxalate ingredients is optimal. When a high moisture diet cannot be provided, increased sodium with a dry diet will also promote dilute urine. Several pet food manufacturers test for low RSS of CaOx in their diets and will indicate which products have

Figure 2. Should struvite crystalluria be treated?



Struvite crystalluria is a common finding that may be inconsequential. Struvite crystals will readily form in urine that is not analyzed immediately, so artifacts are common. Because dogs form struvite stones in conjunction with urinary tract infections, crystalluria alone does not require treatment. Overall it is more important to manage clinical signs of lower urinary tract (LUT) disease and perform diagnostics as needed.

low RSS for struvite and CaOx. Choosing diets labeled with low RSS for CaOx is recommended. Homemade diets are also high in moisture and may be formulated by veterinary nutrition specialists (diplomates of the American College of Veterinary Internal Medicine (Nutrition) or the European College of Veterinary and Comparative Nutrition) if patients have concurrent diseases that limit the use of stone-prevention diets.

Struvite Dissolution

Since dogs nearly always have urinary tract infections that facilitate struvite stone formation, dietary therapy is primarily aimed at dissolution. Choosing high moisture diets with controlled levels of magnesium and phosphorus and with moderate amounts of protein can aid dissolution with appropriate antimicrobial therapy. As with CaOx stones, higher sodium content can lower urine concentration when a high moisture diet cannot be provided. Products labeled with a low struvite RSS can help with dissolution and may be continued long-term for the rare sterile struvite or to lessen the chance of stone formation with intractable UTIs. Use caution when recommending diets labeled for struvite dissolution since some do not contain appropriate protein levels for long-term use.

SUMMARY

Although most struvite stones are infection-based, diet plays a role in the management of both struvite and CaOx stones in dogs. While a urinary diet is fed, treats should be limited to less than 10% of calorie intake. Ideally, any treats should be labeled as having RSS values compatible with stone prevention. Low oxalate fruits and vegetables such as broccoli, cauliflower, zucchini, bananas, and applesauce also make great low-calorie treats. After starting a dog on a urinary diet,

patients with CaOx stones should be monitored with urinalysis to assess urine specific gravity to make sure urine remains dilute at approximately 1.020 or less. In dogs with struvite urolithiasis, urine specific gravity should be assessed as well as the presence of white blood cells on sediment analysis, which may indicate UTI and the need for urine culture. Dogs should also be evaluated with radiographs or ultrasound during struvite dissolution to ensure complete dissolution occurs. For all stone types, veterinary team members should discuss whether urinary signs such as stranguria or hematuria are present, as the presence of clinical signs is also a useful tool in monitoring dogs with urolithiasis.

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URATE UROLITHIASIS IN DOGS

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KEY TAKEAWAYS

- Hyperuricosuria (HUU) is characterized by elevated urinary uric acid concentrations, which is one risk factor for bladder or kidney stone formation.
- Most dogs with HUU and urate urolithiasis can be managed with a purine restricted, high moisture diet.
- Dogs can also develop urate urolithiasis as a result of liver diseases such as portovascular shunts, and occasionally microvascular dysplasia.

EPIDEMIOLOGY AND PATHOPHYSIOLOGY

Urate uroliths are the third most common urolith submitted from dogs from the US and UK to urinary stone analysis laboratories,[1-3] and the proportion of urate uroliths submitted to the G.V. Ling Urinary Stone Analysis Laboratory in Davis, California, USA for analysis has not changed in the past ten years,[1,2] suggesting that strategies for prevention based on known risk factors are not effectively decreasing submissions to laboratories. Most urate uroliths are removed from the lower urinary tract, but they can also occur in the upper urinary tract (kidney, ureters) of dogs. Hyperuricosuria (HUU) has an autosomal recessive mode of inheritance. A mutation in *SLC2A9* gene has been found to be associated with HUU in dogs. Most commonly, dogs develop urate uroliths due to this *SLC2A9* gene mutation, which was identified as the underlying defect in Dalmatians and many other unrelated breeds.[2] Dogs with the *SLC2A9* gene mutation have HUU, a risk factor for urate urolithiasis.[4] A DNA test for the *SLC2A9* mutation can determine the genetic status of dogs for HUU (https://vgl.ucdavis.edu/test/hyperuricosuria). Dogs that carry two copies of the mutation will be affected and susceptible to develop urate urolithiasis. Dogs can also develop urate urolithiasis as a result of liver diseases such as portovascular shunts, and occasionally microvascular dysplasia. The HUU breeds, such as the Dalmatian, English Bulldog, and the American Pitbull Terrier, as well as dogs with liver disease do not metabolize endogenous and ingested purines to allantoin, which has a high water solubility (**Figure 1**). This lack of hepatic conversion of uric acid by intracellular uricase to allantoin results in HUU. This, combined with concentrated urine and acidic urine, are the predominant factors that predispose to urate urolith formation.

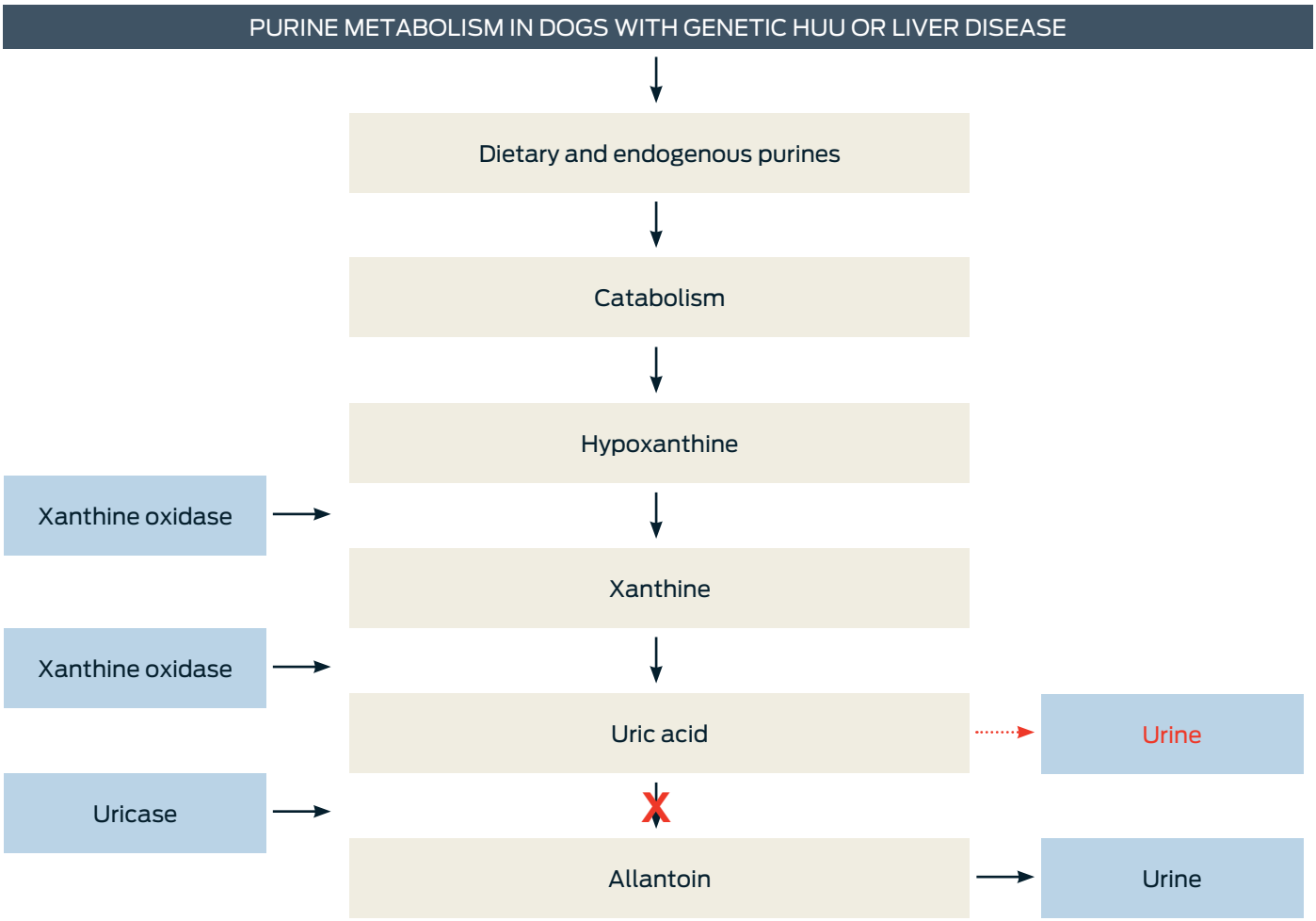
SIGNALMENT AND CLINICAL SIGNS

Urate-containing uroliths were submitted more often from dogs < 7 years of age compared with older dogs, and over one-third were submitted from dogs between 4 and 7 years of age.[2] While some laboratories have reported more urate uroliths removed from male dogs, others reported urate-containing uroliths were more common in female dogs.[2] These differences might be due to how the layered stone analyses are reported among laboratories. In dogs with congenital portovascular anomalies, urate uroliths can be found incidentally, especially in young dogs prior to spay or neuter, or during the diagnostic work up for clinical signs suggestive of the liver disorder (e.g., depression, vomiting, neurological signs). In dogs with urate cystoliths, clinical signs such as pollakiuria, hematuria, stranguria, or even urethral obstruction in male dogs might be present. Acute kidney injury might also be noted in dogs with ureteral obstruction or nephrolithiasis.

DIAGNOSTICS

A CBC and serum biochemical panel should be evaluated, particularly for dogs with suspected liver disorders. These baseline data are also warranted to screen for comorbidities that might alter dietary strategies for urate urolithiasis prevention in dogs

Figure 1. Purine metabolism in dogs with genetic HUU or liver disease
HUU = hyperuricosuria



with genetic HUU. A urinalysis should be submitted, particularly to obtain a baseline urine specific gravity. Ammonium biurate crystals might or might not be present on urine sediment examination. Evidence of ammonium biurate crystalluria in non-HUU breeds warrants further diagnostics for hepatic disease such as a portovascular anomaly. A urine culture should be submitted in dogs prior to any surgical or minimally invasive procedures for urolith removal. Urate uroliths are only slightly radiodense or might be radiolucent, and ultrasonography, contrast cystourethrograms, or cystoscopy are considered more sensitive for detection of uroliths. Radiography was only able to detect 32% of cases with urate uroliths in one study, with many more dogs that required contrast cystourethrograms for detection.[5] Ultrasonography is also valuable in order to assess the dog for any evidence of microhepatica, or an obvious portovascular shunt as well as for evidence of ureteral obstruction in dogs with upper tract urate urolithiasis.

MANAGEMENT

Management of urate urolithiasis can be multimodal, with medical or surgical interventions or likely a combination of the two, and prevention of urate urolithiasis once the stones have been removed has dietary and potentially additional medical components (**Figure 2**). Urate solubility increases with increasing urinary pH, and dissolution may be considered for dogs with genetic HUU with urate urolithiasis so long as there is no evidence of ureteral or urethral obstruction.[6] In one study, administration of a ultra-protein restricted (and therefore purine-restricted) diet and the xanthine oxidase inhibitor, allopurinol, to a small number of Dalmatians with urate urolithiasis was effective for 40% of the dogs.[7] Dissolution has not been reported for dogs with underlying liver disorders, and allopurinol should not be administered to these dogs.

In dogs with clinical urate urolithiasis, minimally invasive (e.g., voiding urohydropropulsion, laser

lithotripsy, basket removal) urolith removal should be considered if appropriate for the dog and client.[8] This decision will depend on the size of the dog, size and number of the uroliths, and necessary equipment that is available to the veterinarian. Otherwise, a cystotomy for cystoliths or subcutaneous ureteral bypass or ureteral stents for obstructive upper tract urate uroliths can be performed.

DIETARY PRINCIPLES FOR PREVENTION

For dogs with portovascular anomalies, cystoliths should be removed at the time of portosystemic shunt (PSS) correction. This should prevent further formation of uroliths. In dogs where surgery is not possible, nutritional management for liver disease should adequately address the necessary principles for urate urolith prevention. Due to the high recurrence rate of urate uroliths in dogs with genetic HUU, multiple strategies for urolith prevention should be implemented. Decreasing the urinary concentration of calculogenic substances by increasing urine volume is one of the cornerstones of urolithiasis prevention.[9] High-moisture (> 75% water) foods should be recommended. Alternatively, sufficient water, 1:1 volume ratio with water and dry food, can be added to dry kibble to increase moisture intake and urine output. While guidelines suggest aiming to achieve a urine specific gravity consistently ≤ 1.020 in dogs, some dogs might require further urine dilution while others will respond well within the suggested urine specific gravity range.[8]

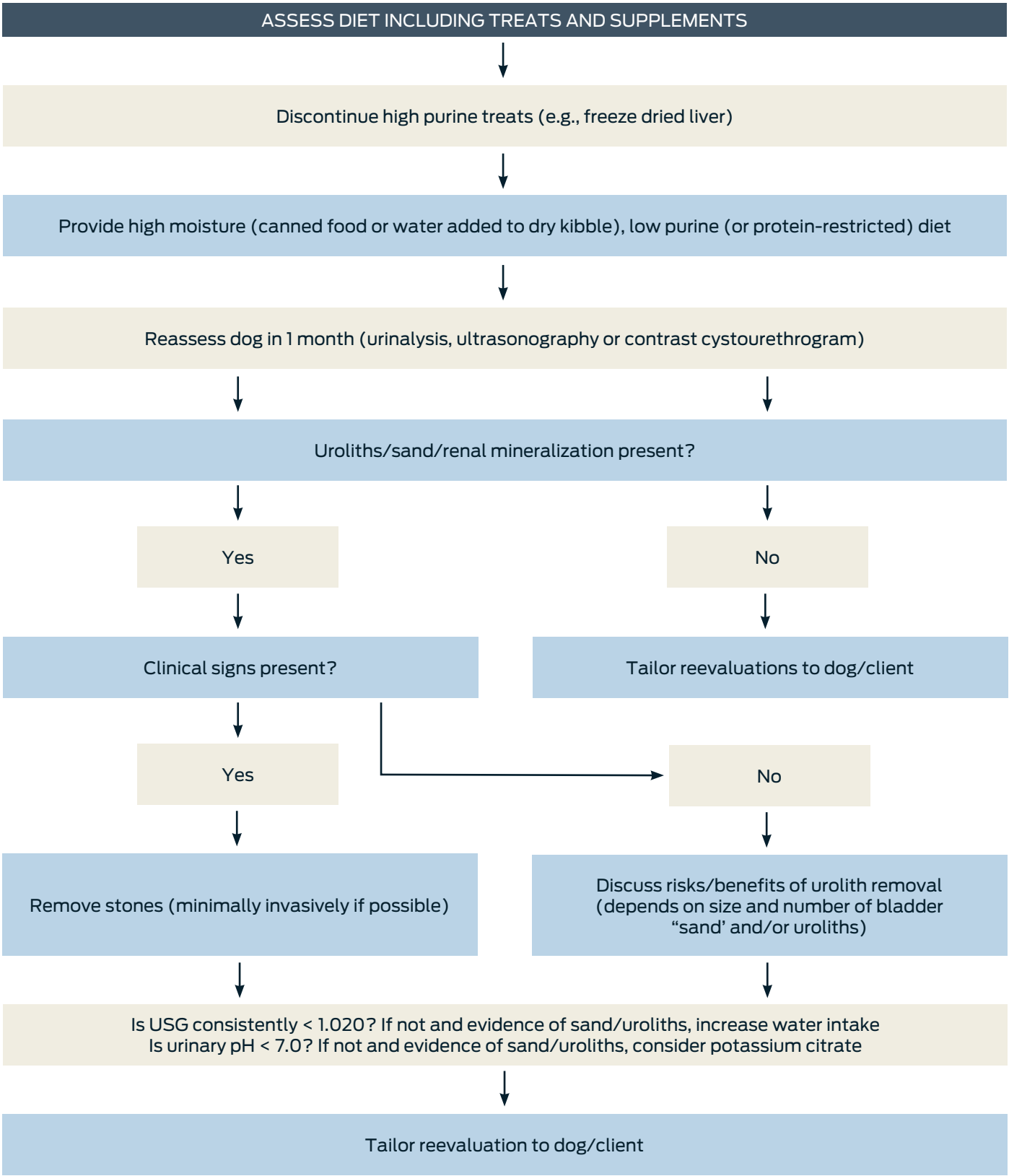
Both AAFCO and FEDIAF recommend that diets formulated for adult dogs contain no less than 45 g protein/1,000 kcal (4.5 g/100 kcal or 18% dry matter basis [DMB]) (FEDIAF MER = 110 kcal x $BW^{0.75}$).[10,11] Purines, a component of DNA, are found in high concentration in common protein sources, although some protein sources, particularly fish and organ meats, contain more than others. Therefore, low protein diets (approximately 3 g/100 kcal; 14% DMB) are often recommended in order to decrease concentrations of urinary purine metabolites. This strategy can be effective but can lead to protein malnutrition if the animal is not eating enough food to meet its daily energy needs. Therefore, higher protein (approximately 5 g/100 kcal or 20% DMB), low purine foods are also marketed for this disease. Vegetarian and hydrolyzed vegetable protein diets might also be considered. If owners wish to provide treats for their dogs, vegetables and dairy proteins have the lowest purine levels. Food sources that are low in uric acid such as strawberries, melons, bananas, peeled cucumbers, and cottage cheese are options, and the caloric content and body condition score of the pet should be considered when recommending treats. There is a lack of literature in dogs with clinical urate uroliths to evaluate the efficacy of these dietary recommendations for preventing ultrasonographic and clinical recurrence of urate uroliths.

COMMUNICATION TIP

"Most dogs with hyperuricosuria and urate urolithiasis can be managed with appropriate dietary therapy which includes a high moisture, low purine diet."

In short-term trials in healthy Beagle dogs, a casein-based diet formulated with 1.9 g protein/100 kcal (10.4% DMB) and 1% potassium citrate (DMB) significantly decreased the urinary activity product ratios of uric acid, sodium urate, and ammonium urate as well as 24-hour urinary uric acid excretion compared with a meat-based diet with 5.7 g protein/100 kcal or 31.4% DMB.[12] Nine dogs with genetic HUU evaluated over a one-year period fed a higher protein (approximately 5 g/100 kcal) purine-restricted dry diet with additional water had a significant decrease in 24-hour urinary uric acid concentration noted at 6 and 12 months compared with their baseline values.[13] However, no differences were noted with other analyzed purine metabolites. While consuming this purine-restricted diet, most of these dogs had mild and occasionally moderate amounts of echogenic bladder "sand" (< 2 mm) or stones (2–3 mm in size) noted in almost every dog at each visit and static renal mineralization on ultrasonographic examination without apparent clinical signs. One exception was a dog that developed cystic calculi, but the owner did not adhere to the dietary recommendations. All dogs in that study were managed without medications such as urinary alkalinizing agents or xanthine oxidase inhibitors while consuming this purine-restricted diet. It is unknown if lowering urinary uric acid excretion any further would have been of additional benefit in these dogs.

Figure 2. Suggested algorithm for urate urolithiasis management of dogs with genetic HUU



Aciduria is considered a risk factor for urate urolithiasis because ammonium and hydrogen ions may precipitate with uric acid.[7] Urate solubility increases with increasing urine pH. Although the solubility of ammonium urate is thought to plateau at pH ≥ 7.2, in vitro dissolution occurred at a pH = 8.0.[8] However, in the clinical trial evaluating dogs consuming the higher protein purine-restricted diet, urinary pH analyzed by urine dipstrip or pH meter was significantly lower among study visits when evaluating spot urine samples at each time point compared with baseline (12-month mean urinary pH: 5.61 ± 0.44 (strip); 5.73 ± 0.26 (meter).[13] Urine pH evaluated by pH meter from the 24-hour pooled urine samples from these dogs was not significantly different among study visits. These values were lower than historically recommended[7] for urate urolithiasis management at all visits, regardless of methodology. The dogs remained free of clinical urolithiasis, although ultrasonographic evidence of "sand" and small cystoliths were present in most dogs.[13] Urinary alkalinizing agents such as potassium citrate could be considered to increase the urine pH, although studies suggest supplementation in healthy dogs may have inconsistent effects on urinary pH.[14]

LONG-TERM MANAGEMENT AND MONITORING

Because dogs with urate uroliths can develop recurrent uroliths of differing mineral composition, any subsequent uroliths should be removed and submitted for analysis to aid in management, regardless of history and presence or type of crystalluria. If recurrent uroliths or urinary mineralization occurs in a dog with known genetic HUU, radiographs and ultrasound together are warranted in order to assist in mineral identification. Urine pH, preferably several spot evaluations or 24-hour pooled samples, should also be evaluated to help tailor management strategies. Reevaluations of dogs should be tailored to the individual patient. Ideally, a urinalysis paying close attention to urine specific gravity, urinary pH, and sediment should be examined approximately 1 month after the dog is transitioned onto the recommended diet. Ultrasound, including the lower and upper urinary tract, is also recommended to evaluate for urolith recurrence. If small uroliths are detected, the benefits and risks of urolith removal should be discussed with the owner, and reevaluations scheduled accordingly. If ultrasound examination reveals more than just moderate sand within the urinary bladder, a voiding urohydropropulsion should be performed, if possible, dietary and hydration recommendations altered, and reevaluations scheduled again in 4–6 weeks. In dogs with portovascular anomalies that are surgically corrected, long-term monitoring for urolith recurrence is likely not necessary. If surgery cannot be performed, periodic monitoring, including a serum biochemical panel, urinalysis, and imaging, should be considered, depending on the dog's clinical signs. Reevaluations should be tailored to the individual dog and performed until adequacy of the current strategy is assessed.

ADJUNCT TREATMENT: XANTHINE OXIDASE INHIBITORS

If dogs have failed therapeutic dietary interventions with appropriate urine dilution, adjunct therapy with the xanthine oxidase inhibitor, allopurinol,[8] can be considered. The pharmacokinetics after oral administration of allopurinol to eight dogs varied greatly.[15] Because of this and the varying magnitude of urinary uric acid excretion among dogs with genetic HUU, the dosage should be titrated based on 24-hour urinary uric acid excretion. However, this is not practical for most veterinarians to perform, and dogs should be monitored for recurrence of uroliths via ultrasonography. To minimize the risk of xanthine uroliths, this drug should only be administered to dogs that are consuming a purine-restricted diet. Should any new uroliths develop while the dog is being administered allopurinol, the uroliths should be removed and submitted for quantitative analysis. A serum biochemistry panel should be monitored every 6 months. If xanthine uroliths develop, the dosage of allopurinol should be decreased or the drug discontinued. Allopurinol should not be administered to dogs with hepatic disease.

CONCLUSION

Hyperuricosuria (HUU) is inherited as a simple autosomal recessive defect. A mutation in the *SCL2A9* gene has been found to be associated with HUU in dogs, which is a risk factor for urate uroliths. However, the *SCL2A9* mutation is not the sole cause of urate uroliths in dogs, and diagnostics for hepatic diseases should be considered if clinically indicated. Most dogs with HUU and urate urolithiasis can be managed with appropriate dietary therapy which includes a high moisture, low purine diet. If recurrent uroliths

develop despite achieving a low urine specific gravity, ideally consistently < 1.020, and alkaline pH with the prescribed diet, allopurinol administration can be considered. In dogs that develop urate uroliths secondary to a portovascular anomaly, correction of this problem should prevent recurrent uroliths. If this cannot be performed, nutritional management for liver disease should adequately address the necessary principles for urate urolith prevention.

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PURINA Institute

Advancing Science for Pet Health

RENAL DISEASE

CHRONIC KIDNEY DISEASE IN CATS

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KEY TAKEAWAYS

- Weight loss and poor body condition are associated with a poorer prognosis in chronic kidney disease (CKD). Ensuring adequate caloric intake and maintaining body weight is therefore a crucial part of CKD management as inappetence is common in these patients.
- Dietary therapy needs to be tailored to the individual cat. Recent advances in renal diet formulations provide an array of protein and phosphorus contents to aid in this endeavor.

OVERVIEW

Nutritional management of CKD is intended to achieve four specific goals: 1) ameliorate or prevent clinical consequences of CKD including signs of uremia; 2) slow progression of CKD and prolong survival; 3) minimize derangements of electrolyte, calcium and phosphorus, and acid–base balance; and 4) maintain adequate caloric intake. To achieve these multifaceted goals, renal diets are typically formulated to have reduced phosphorus content; modified amounts of high-quality protein; increased caloric density; added B vitamins; increased omega-3 polyunsaturated fatty acid, antioxidant, and amino acid content; potassium supplementation; and to have a neutral effect on acid–base balance. Clinical trials have supported clinical benefits of "kidney diets" formulated similar to these dietary modifications.[1-5]

KEY NUTRIENTS

Phosphorus

As kidney disease progresses, appropriate processing of phosphorus and calcium declines, resulting in phosphorus retention and causing parathyroid hormone (PTH), fibroblast growth factor 23 (FGF23), and calcitriol to become dysregulated. Together with their associated clinical manifestations, this is referred to as CKD-Mineral Bone Disorder (CKD-MBD).[6-9] Mechanisms involved in CKD-MBD are different between early and late stages of CKD. Phosphorus retention is a key mediator in CKD-MBD if intake is not decreased. In early disease, phosphorus retention triggers production of the phosphaturic hormone FGF23 which acts to decrease phosphorus by downregulating transporters responsible for phosphorus regulation in proximal tubules, decreasing phosphorus absorption from the gastrointestinal tract indirectly, and by inhibiting PTH secretion. In early CKD when nephron mass is sufficient to excrete phosphorus adequately, these actions are able to control phosphorus retention. As CKD progresses, FGF23 no longer adequately mitigates phosphorus retention due to the low number of functioning nephrons, stimulating PTH synthesis and leading to renal secondary hyperparathyroidism. At this juncture the control of dietary phosphorus intake becomes critical.

Most maintenance diets contain substantial quantities of phosphorus, with the protein source typically contributing significantly to the phosphorus content. The source of the phosphorus (organic vs. inorganic), as well as the calcium to phosphorus ratio, are important to consider. Phosphorus from inorganic sources (sodium or potassium phosphate salts) is more bioavailable than organic phosphorus (meat, bone meal, grains). Feeding a diet with highly bioavailable phosphorus salts in combination with too little calcium can result in renal damage.[10] Based on our current knowledge, a calcium to phosphorus ratio of 1.1–1.4 is a reasonable goal.[11] Unfortunately it is not currently possible for the clinician or caregiver to determine which source of phosphorus is used in a particular diet or treat. Determining the exact amount of dietary phosphorus intake is challenging as well, and can be complicated by owners giving unbalanced treats, table scraps, and foods for medication administration. This is a developing area of study.

Dietary therapy may take several weeks to have a discernible effect on serum phosphorus concentrations; in one study full dietary effect was apparent after 28–49 days.[12] Thus, serum phosphorus concentrations should be rechecked 4–6 weeks after initiating the renal diet. If in the IRIS target range (serum phosphorus should be less than 4.5 mg/dL [1.5 mmol/L] for IRIS Stage 2 and 3 and less than 6.0 mg/dL [1.9 mmol/L] for IRIS Stage 4), the diet should be continued, and the serum phosphorus reassessed every 3–4 months (every 4–6 months may be adequate for IRIS CKD Stage 2). Control of phosphorus is more likely achieved with renal diet alone in patients with Stage 2 and 3 CKD. If a renal diet alone fails to achieve the serum phosphorus target after 4–6 weeks, adding an intestinal phosphorus binding agent is recommended.

Protein

It is perhaps a common misconception that the purpose of renal diets is protein restriction. There is little consensus on the appropriate amount of protein in renal diets, but there is a significant amount of evidence regarding the importance of phosphorus restriction.[8,11] Recently, early-stage renal diets that are phosphorus restricted but less protein restricted have also become available for cats, so tailored therapy for individual patient needs is possible. All diets for cats with CKD should contain high-quality, highly digestible protein. Evidence suggests that increased dietary amino acid concentration rather than increased total protein content adequately supports maintenance and/or slows loss of lean muscle mass.[4]

Potassium

Inadequate dietary intake, increased urinary loss, and activation of the renin-angiotensin-aldosterone system (RAAS) are all thought to contribute to hypokalemia in feline CKD. Hypokalemia is associated with development and worsening of CKD in humans and appears to exacerbate damage to tubular epithelial cells.[13] Serum potassium levels are not representative of systemic tissue potassium levels, and cats with low normal serum potassium may actually be systemically depleted, particularly in conjunction with metabolic acidosis.[14] Potassium is vital for normal muscle function and GI motility, and supplementation has been demonstrated to correct hypokalemic myopathy. Some clinicians recommend supplementation even when serum potassium is in the low normal range, with a goal of maintaining serum potassium levels above 4 mmol/L, but the effect on the progression of CKD has not been evaluated. As cats are challenging to medicate, the amount of dietary potassium should always be evaluated. Feline CKD diets are supplemented with potassium, and a diet higher in potassium may have the desired clinical effect.

Acid–Base Balance

Metabolic acidosis occurs in CKD due to the inability to excrete acids as kidney function declines.[15] Metabolic acidosis is common in human CKD patients but may not be overtly recognized in feline CKD patients until the late stages of disease depending on how the assessment is made.[15] Therapeutic diets formulated for cats with CKD are typically supplemented with alkalinizing agents to promote acid–base balance.[11]

Fat and Energy Density

Renal diets are typically high in fat and calorically dense to promote adequate energy intake. Maintenance of calorie intake, body weight, and body condition are important goals for cats with CKD.

Hydration

Dehydration is common in CKD due to impaired ability to concentrate urine and can lead to inappetence, lethargy, weakness, constipation, and increased susceptibility to uremic crisis. It may precipitate pathophysiologic responses (RAAS activation, chronic vasopressin release, poor perfusion) that have a negative effect on the kidney. Additionally, it may also exacerbate formation of stones and occurrence of urinary tract infections. In the author's experience, adequately maintaining hydration by giving subcutaneous (SQ) fluids appears to substantially help quality of life and improve appetite and activity. It can be a very helpful tool for caretakers in management of disease but may not be necessary for every patient. The best candidates for SQ fluid therapy (75–150 mL SQ every 1–3 days) are those cats that appear to gain clinical benefit from management of hydration, are prone to secondary complications of chronic dehydration such as constipation, and do not suffer quality of life concerns from the procedure. If possible, supplementation with free water (orally or with a feeding tube) is preferred to avoid the sodium load that comes with the electrolyte solutions available for subcutaneous use (excess sodium should be avoided

in CKD).[11] Feeding canned food instead of dry, adding water to food, or using nutritional supplements to increase water intake are other ways to potentially increase water consumption. Paying special attention to water sources in the house—fresh, accessible, water fountains, etc., is also key.

UTILIZATION OF IRIS STAGING

Based on evidence from clinical studies, IRIS recommends renal diets be considered for cats with IRIS CKD Stage 2 and recommends feeding renal diets to cats with IRIS CKD Stages 3 and 4.[16] As of yet, it is unclear what the recommendation should be in patients with IRIS Stage 1 disease. Recently, hypercalcemia has been documented in some cats with early-stage disease associated with switching to a renal diet, likely due to restricted phosphorus content and/or unbalanced calcium to phosphorus ratio. It appears to be more likely in cats with phosphorus <3.9 mg/dL (1.3 mmol/L) and potassium <3.8 mmol/L.[17] In these instances increasing the amount of phosphorus in the diet by switching diets or feeding 25% of daily calorie intake of a less phosphorus-restricted diet has resulted in resolution of hypercalcemia.[18]

COMMUNICATION TIP

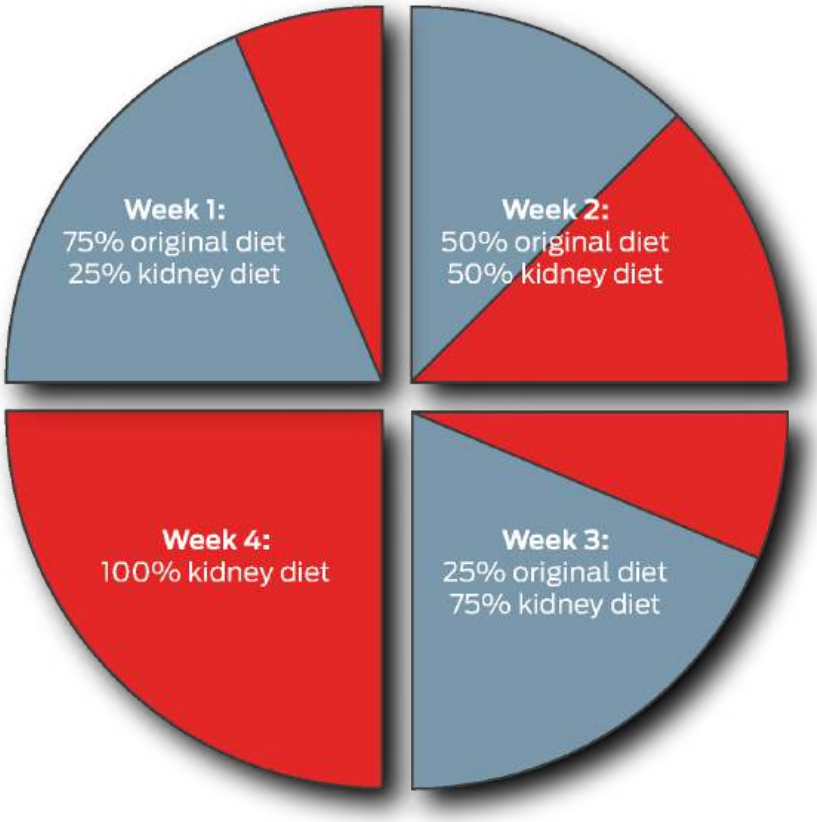
"If the caretakers understand the importance of the kidney diet as a medical intervention, not just a food, they are more likely to comply with the instructions."

TIPS FOR FEEDING MANAGEMENT

As CKD advances, dysrexia and inappetence cause a chronic and insidious decline in calorie intake, overall body condition, and muscle condition. Weight loss is associated with a poorer prognosis in patients with CKD.[19] Additionally, poor appetite is perceived as a significant quality of life concern and can cause significant emotional distress to caretakers.[20] In desperation, many caretakers will offer high-protein foods to their pets in an effort to increase their food intake. Therefore, a key therapeutic target for these patients is determining caloric goals and addressing appetite and food intake to meet that target. The desired outcome is maintenance of body condition and muscle condition, ideally while eating a therapeutic diet formulated for cats with CKD. Many clinicians and caretakers find this goal to be challenging, and the following tips may be helpful for success.

- If the patient was not eating their usual diet prior to presentation, they are unlikely to accept a new diet. Often it is a general inappetence, not dislike of the kidney diets, that make transition difficult. Therefore, identification and management of complications of kidney disease that have the potential to affect appetite such as dehydration, nausea, anemia, hypertension, and electrolyte imbalances are important before attempting a diet transition.
- Similarly, when hospitalized, patients should not be introduced to a kidney diet. They will associate the new food with the stressful surroundings, and food aversion is likely. Wait until the patient is stable and discharged before trying a kidney diet.
- Transition to a kidney diet from the patient's original food over at least 2–4 weeks (**Figure 1**).
- The most important factor in the success of diet transition is the education of the caretaker. If the caretakers understand the importance of the kidney diet as a medical intervention, not just a food, they are more likely to comply with the instructions. Many caretakers will offer the food once, and if the cat refuses, will assume they will never eat a kidney diet. If they realize the importance of a kidney diet, they will put forth the time and effort to transition properly.
- In addition to using tools such as altering food type, presentation style, and temperature, consider the location of meals; all meals should be offered in a secure, easily accessible, familiar environment with minimal distractions or competition.
- Provide small, frequent meals and maximize palatability to encourage intake. Positive reinforcement (petting and praise) should accompany meals.
- Follow-up phone calls (at least weekly) to check on the progress of the caretaker and pet during the transition phase from the original diet to a kidney diet will increase compliance and emphasize the importance of dietary management.

Figure 1. An example protocol for transitioning a cat with CKD to a renal diet



The exact protocol needed will depend on the individual cat. Some cats may readily accept the new diet and allow for a faster transition, while others may need an even slower transition. Appetite stimulants may be helpful to aid transition.

- "Toppers" of senior diets consisting of <10% of daily caloric intake can also be used to stimulate interest in kidney diets. Due to food aversion that may develop as a result of uremia, novelty may encourage food consumption.
- Treats, extras, and foods for medication administration can contribute phosphorus and protein, so these should be kept to <10% of total daily calories, and foods with high phosphorus and protein content should be avoided.
- Anti-emetics and anti-nausea medications such as maropitant and ondansetron may be helpful in managing clinical signs of uremia and improving appetite.[21]
- Appetite stimulants are useful in nutritional management and should be utilized as soon as deficiencies in caloric intake, body condition score (BCS), or muscle condition score (MCS) are documented.[22,23]
  - Mirtazapine (oral or transdermal)
  - Capromorelin (oral)
- If caloric intake is still not adequate, then esophageal feeding tubes (E-tubes) should be considered for long-term management.[24] E-tubes are also very helpful for fluid and medication administration.

MONITORING

Serial evaluations of nutritional status are a key part of CKD patient management, and the nutritional plan should be checked for every patient at every visit, including body weight, BCS, MCS, adequacy of caloric intake, and a complete dietary history. Serum biochemistry, hematocrit, urinalysis (with UPC [urine protein to creatinine ratio] if appropriate) and blood pressure should be monitored within the first month of starting dietary therapy and every 3–6 months thereafter depending on IRIS stage. Monitoring parameters for diet and nutrition in CKD cats are shown in **Box 1**.

CONCLUSION

Recent advances in renal diet formulations provide an array of protein and phosphorus contents to aid in formulating the most appropriate nutritional plan for the patient. The concept is that dietary management, like any other kind of therapy, needs to be tailored to the individual cat.

Box 1. Monitoring parameters for diet and nutrition in CKD cats

Recognizing that there are individual cats at each stage that will need adjustments to their dietary therapy is important. Dietary therapy may need to be adjusted for the individual cat by:

- Increasing caloric intake if weight goals are not achieved.
- Modifying protein content based on nutritional need, BCS, and MCS.
- Increasing phosphorus restriction if serum phosphorus fails to meet the target level through the addition of intestinal phosphate binders.
- Reducing phosphorus restriction and being cautious with the use of products that might exacerbate hypercalcemia.

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CHRONIC KIDNEY DISEASE AND PROTEINURIA IN DOGS

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KEY TAKEAWAYS

- Dogs with CKD and proteinuria should receive a diet based on their IRIS stage to cover all energy and nutrient requirements, including amino acids.
- If anorexia is a concern, using kidney-friendly tactics to increase palatability, appetite stimulants, and feeding tubes may help ensure adequate intake.

DEFINITIONS AND SCOPE

Feeding management of chronic kidney disease (CKD) is a key point in patient survival and quality of life. Dietary water, energy, phosphorus, calcium, amino acids, protein, and electrolytes must be adapted to the physiological changes imposed by the disease. Fiber, omega-3 fatty acids, and anorexia management also need to be integrated into a feeding plan based on International Renal Interest Society (IRIS) staging and degree of proteinuria. Anorexia management and encouraging food intake are important parts of managing dogs with CKD. The overall nutritional plan is summarized in **Figure 1**.

KEY NUTRIENTS FOR THE MANAGEMENT OF CHRONIC KIDNEY DISEASE AND PROTEINURIA IN DOGS

Nutrition is an essential component of management for CKD and proteinuria in dogs.[1] There are several key nutrients that play a role in the health of a dog with renal disease. Many of these nutrients are outlined in this section. Target levels of key nutrients can be found elsewhere.

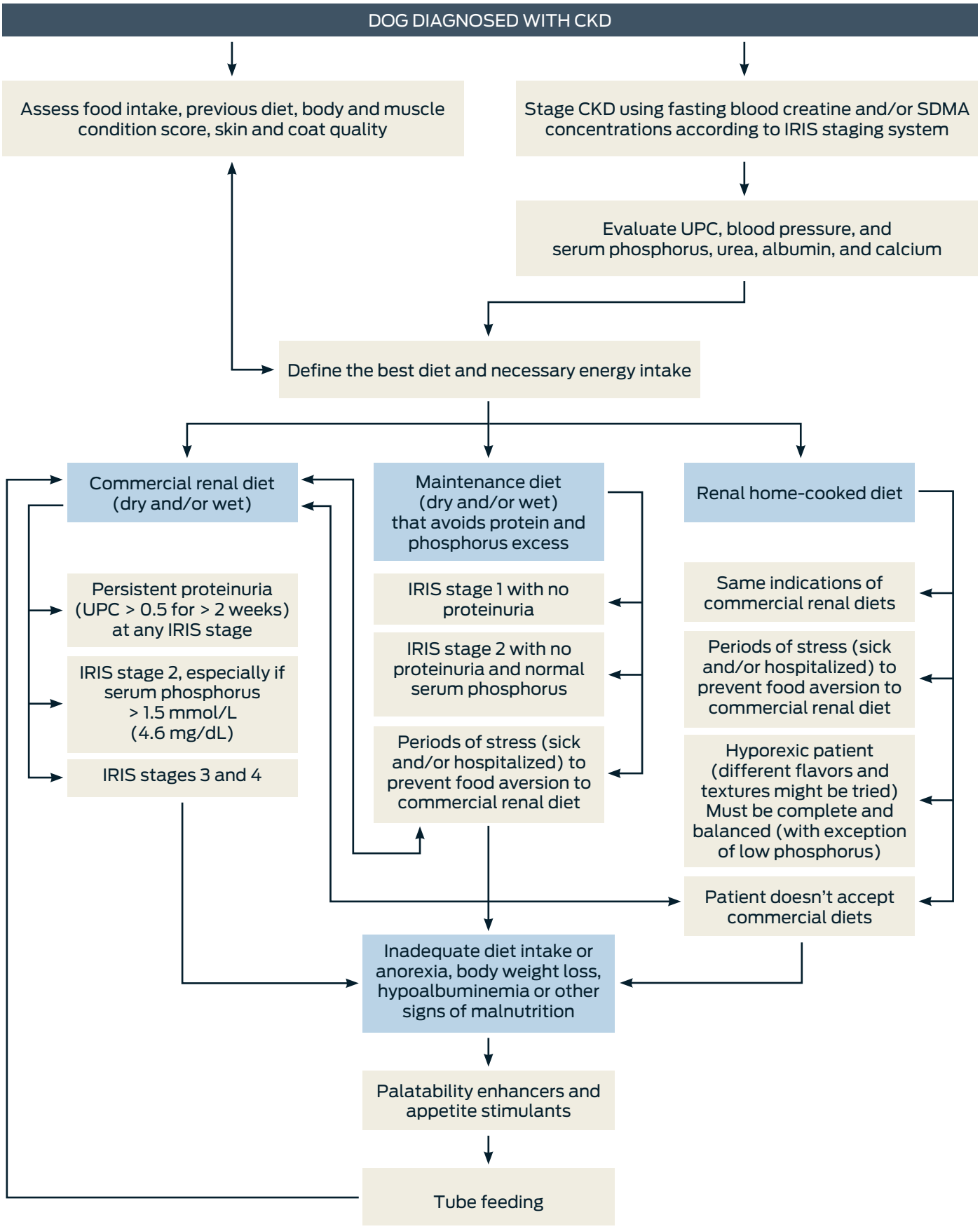
Energy

Sufficient energy must be provided to prevent endogenous catabolism, including protein catabolism, which results in malnutrition and exacerbation of azotemia. However, the energy requirements of dogs with CKD are currently unknown. Recommendations range from 95 to 130 kcal/kg of body weight$^{0.75}$/day but are variable among patients and should be estimated considering body condition and muscle condition score, age, activity level, and the presence of other diseases. Body weight and condition must be reassessed frequently so that the energy supply can be readjusted as needed to promote a healthy body weight. Commercial renal diets are usually energy-dense (dry > 3,900 kcal/kg; wet > 1,300 kcal/kg), allowing patients to obtain their energy needs in a smaller volume of food, minimizing gastric distention, nausea, and emesis.[2] Starch and fat are the main energy sources, minimizing endogenous nitrogen production and azotemia.

Phosphorus

The functional nephron loss in CKD affects the homeostasis of several solutes, including phosphorus. Phosphorus retention (hyperphosphatemia) inhibits calcitriol formation in the kidney and stimulates parathyroid hormone (PTH) secretion, causing secondary renal hyperparathyroidism (SRHP), which may lead to bone demineralization and soft tissue (including kidney) mineralization.[3] Evidence suggests that chronic reduction of phosphorus intake to maintain plasma phosphorus concentration below 1.5 mmol/L (but not less than 0.9 mmol/L; < 4.6 mg/dL but > 2.7 mg/dL) can be beneficial to patients with CKD,[4] as it increases patient survival[1,5] and may prevent SRHP development. Commercial renal diets are phosphorus restricted below the recommended allowance or minimum nutrient recommendations published by AAFCO and FEDIAF for healthy adults, to help normalize serum phosphorus concentration. Phosphorus restriction must be the first approach to control hyperphosphatemia. If after dietary restriction phosphate remains high, IRIS (2023) recommends the use of enteric phosphate binders (aluminum hydroxide, aluminum carbonate, calcium carbonate, calcium acetate, or lanthanum carbonate) to effect and mixed with each meal (**Box 1**).

Figure 1. Algorithm for nutritional recommendations for dogs with CKD and proteinuria
CKD = chronic kidney disease; SDMA = symmetric dimethylarginine; UPC = urine protein:creatinine ratio



Box 1. Using canine IRIS staging guidelines to make diet recommendations

IRIS (2023) treatment recommendations follow the CKD staging and treatment recommendations, based on blood creatinine or SDMA concentration, serum phosphorus and proteinuria based on urine protein:creatinine ratio (UPC) assessed on at least two occasions in a hydrated, stable patient on at least two urine samples collected two or more weeks apart, and multiple systolic blood pressure determinations, preferably done during repeated patient visits on separate days or during the same visit with at least 2 hours separating determinations:[4,18]

- **Stage 1:** Normal blood creatinine (< 125 µmol/L or < 1.4 mg/dL) and/or normal or mild increase in blood SDMA (< 18 µg/dL), along with some renal abnormality (abnormal renal palpation or imaging findings, renal proteinuria, abnormal renal biopsy). At this stage, a renal diet is only recommended if the patient has renal proteinuria (UPC > 0.5) for more than 2 weeks. In this situation, the renal diet needs to be combined with angiotensin-converting enzyme inhibitor (ACEI) utilization.
- **Stage 2:** Mildly increased creatinine (125–250 µmol/L or 1.4–2.8 mg/dL), mild renal azotemia, mildly increased SDMA (18–35 µg/L), and mild or absent clinical signs. The use of a renal diet is recommended particularly if the patient has persistent renal proteinuria (UPC > 0.5 for more than 2 weeks) or serum phosphorus greater than 1.5 mmol/L (4.6 mg/dL). If phosphorus remains high after dietary restriction, enteric phosphate binders are recommended. Renal diets are often suggested in Stage 2, regardless of phosphorus concentration and UPC level, considering that dogs are often more willing to accept and become accustomed to the renal diet in this stage.
- **Stage 3:** Moderate renal azotemia, creatinine values between 251–440 µmol/L (2.9–5.0 mg/dL), and SDMA between 36–54 µg/L. Extrarenal signs are usually present, but their extent and severity may vary. A renal diet is recommended regardless of UPC and serum phosphorus. If the serum phosphorus concentration remains above 1.6 mmol/L (5.0 mg/dL) after dietary restriction, enteric phosphate binders should be given.
- **Stage 4:** Increased risk of systemic clinical signs and uremic crises, creatinine above 440 µmol/L (5 mg/dL), and SDMA above 54 µg/L. A renal diet is recommended regardless of the values of UPC and serum phosphorus. If the serum phosphorus concentration remains above 1.9 mmol/L (6.0 mg/dL) after dietary restriction, enteric phosphate binders should be given. A long-term feeding tube (esophageal or gastrostomy tube) can help prevent and manage protein/calorie malnutrition and dehydration.

Calcium and Vitamin D

Dogs with CKD may develop hypo- or hypercalcemia, but the incidence may vary if ionized versus total calcium is considered.[6] Hypocalcemia may occur due to calcitriol deficiency as a consequence of renal tissue loss and/or to inhibition of synthesis secondary to hyperphosphatemia. On the other hand, hypercalcemia pathophysiology is incompletely understood but may be associated with reduced urinary excretion of calcium, increased bone turnover, calcium intake exceeding the renal excretion capacity, and/or higher tubular calcium reabsorption due to PTH increase.[6] Most commercial renal diets have higher calcium concentrations, with a calcium to phosphorus ratio of 2:1, aiming to control SRHP and to reduce intestinal phosphorus absorption; the formed calcium-phosphorus complex is insoluble. However, if the patient develops hypercalcemia, a reduction in calcium intake is necessary and, in some cases, may necessitate use of a properly formulated calcium-restricted home-cooked diet.

Protein and Amino Acids

The protein requirements of dogs with CKD remain unknown. Reduction in protein intake has long been recommended to control clinical signs of uremia (nitrogenous metabolite accumulation, derived from dietary and endogenous protein degradation), proteinuria, gastric hyperacidity, anemia, polyuria, and polydipsia. Protein restriction, however, is controversial, as protein intake influences lean body

COMMUNICATION TIP

It is important to closely monitor food intake. If inadequate, ideas for increasing food intake include palatability enhancers appropriate for CKD or proteinuria, appetite stimulants, and feeding tubes.

mass and diet palatability, and protein malnutrition is associated with patient morbidity and mortality.[7] Additionally, CKD is more frequent in older dogs, and older animals may already present with reduced muscle mass and function (sarcopenia) before developing CKD. Commercial renal diets have reduced protein content but still supply or exceed essential amino acid recommendations for dog adult maintenance to avoid protein malnutrition. The rationale is that a controlled reduction in nonessential protein may decrease nitrogenous waste production, ameliorating or controlling the clinical signs of uremia but not altering renal function.[8] Protein restriction is also recommended as a dietary intervention in proteinuric CKD dogs (urine protein/creatinine ratio [UPC] > 0.5 for more than 2 weeks)[3] to help reduce proteinuria, improve glomerular filtration rate, and decrease structural damage to the remaining glomeruli.[7] For protein restriction to be beneficial, however, patients need to consume adequate quantities of essential amino acids and must consume their maintenance energy requirement to prevent endogenous protein catabolism. This can be significantly influenced by diet palatability.

Sodium

Although healthy dogs are generally not salt sensitive, high salt intake may produce adverse consequences in some CKD patients and should be avoided.[9] According to the IRIS Treatment Recommendations for CKD in Dogs (2023), however, there is no evidence that a lower dietary sodium will reduce blood pressure. If attempted, lowering dietary sodium should be accomplished gradually and in combination with pharmacological therapy for hypertension, as a rapid reduction in sodium intake may cause dehydration and volume contraction, with the potential to precipitate a renal crisis.[10]

Potassium and Magnesium

Dogs with CKD may develop hypo- or hyperkalemia. Hypokalemia results from renal potassium loss (related to polyuria), anorexia, vomiting and diarrhea. Hyperkalemia may occur due to the use of medications that influence the renin–angiotensin–aldosterone system (angiotensin-converting enzyme inhibitors, angiotensin receptor antagonists) or potassium dietary intake exceeding the renal excretory capability. Dietary potassium intake can be adjusted in both cases to control serum concentration.[11] Properly formulated potassium-restricted home-cooked diets may be necessary in cases of hyperkalemia.

Hyper- or hypomagnesemia may also develop. In humans, hypomagnesemia can occur due to tubular damage resulting in impaired magnesium resorption; conversely hypermagnesemia may occur due to severe glomerular dysfunction in patients with a marked reduction in glomerular filtration rate. Further research on the role of magnesium in dogs with CKD is needed.[12]

Omega-3 Fatty Acids

Omega-3 (n3) polyunsaturated fatty acid supplementation has been shown to help reduce proteinuria and production of pro-inflammatory eicosanoids, decrease glomerular hypertension, and maintain glomerular filtration rate (urinary clearance of exogenous creatinine). A dose of 140 mg of eicosapentaenoic acid (EPA) plus docosahexaenoic acid (DHA) per kg of body weight$^{0.75}$ per day is suggested as adjunctive dietary treatment for dogs with CKD, but it can be increased depending on the severity and chronicity of the disorder up to the NRC safe upper limit (370 mg of EPA plus DHA per kg of body weight$^{0.75}$ per day).[13] If oral supplementation is recommended, the clinician must calculate the amount of EPA and DHA provided by the diet and the EPA and DHA concentration in the supplement.

Fiber

Fermentable fiber and prebiotics have been suggested for patients with CKD to modulate gastrointestinal health, promoting proliferation of beneficial colonic bacteria that may use intraluminal nitrogen and urea, resulting in lower absorption of these compounds. The bacteria may also increase fecal nitrogen excretion, which has been suggested to reduce blood urea concentrations.[10] Diets with 3% to 4% crude fiber on a

dry matter basis (0.75–1 g/100 kcal), or approximately 10% to 12% total dietary fiber (2.5–3 g/100 kcal) with a moderately fermentable source may be used to help achieve these benefits. However, the bacterial use of ammonia is unlikely to reduce these toxins. No study documenting these changes has been reported.[10] It is important to note that excess dietary fiber may affect diet palatability and reduce the energy density of the diet, which can prevent weight gain if needed.

PROTEINURIA

Proteinuria may be present in any stage of CKD in dogs. Although proteinuria represents a direct protein loss through the kidneys, its nutritional implication has not been thoroughly explored. Protein loss may cause protein malnutrition and hypoalbuminemia in the patient.[14,15] Proteinuria control is important in order to avoid the loss of this key nutrient through urine and because protein can exacerbate the damage to glomeruli and nephrons and worsen CKD progression. In dogs, reduction in protein intake alone failed to prevent proteinuria and CKD progression.[16] Reducing protein intake, in combination with moderate sodium, supplementation with EPA ahd DHA, and medical management of hypertension (if needed), can help manage the patient.[17] If serum albumin is < 20 g/L (2.0 g/dL), IRIS (2023) also recommends low doses of clopidogrel to help reduce hypercoagulability.

TIPS FOR FEEDING MANAGEMENT IN DOGS WITH CKD AND PROTEINURIA

Active monitoring of food intake, body weight, and body and muscle condition score are necessary for early recognition of a possible deterioration in nutritional status. The adjustment of diet nutrient profile to compensate for the metabolic alterations in CKD, and strategies to ensure energy intake, are relevant aspects to patient quality of life and longevity.

Dietary Management in Stress Periods

Renal diets should never be offered to a patient when hospitalized or sick because of the high risk of developing food aversion. Although this can be a bigger risk in cats, it is a problem in dogs as well. This could result in decreased food acceptance even when the patient is feeling better. One option would be to feed a patient a commercial maintenance food that avoids protein and phosphorus excess or a home-cooked diet that is properly formulated for dogs with CKD short-term. The renal diet should be gradually implemented when the patient is stable and comfortable at home.

Hydration

Patients with CKD have polyuria due to reduced urine concentrating capacity caused by functional nephron loss. This polyuria is compensated by polydipsia; however, if the water loss exceeds the intake, the patient may develop dehydration. IRIS (2023) recommends ensuring that patients have fresh, clean drinking water available at all times. If the patient becomes ill for any reason, and if additional fluid loss or lower fluid intake occurs, intravenous or subcutaneous fluid therapy with isotonic, polyionic fluid replacement is mandatory to correct dehydration/hypovolemia. The fluid choice must be guided by monitoring the patient's fluid and electrolyte balance.

Diet Transitions

Any diet changes should be gradually made over the course of 2 weeks to avoid food aversion. Some patients may require a shorter or longer transition depending on appetite, food acceptance, and the presence of concurrent disease.

Treats

If the patient is receiving a large quantity of treats with high phosphorus and protein content (e.g., meat, such as chicken breast or sausage, or dairy), modification of the treats alone may sufficiently decrease the animal's phosphorus and protein intake. Treats should be provided at no more than 10% of total daily calories, but the phosphorus and protein content should be monitored regardless.

Management of Anorexia

Patients with CKD usually present with episodes of hyporexia or anorexia, depending on CKD stage. Uremic toxin retention, dehydration, biochemical alterations (azotemia, metabolic acidosis, electrolyte imbalances, and mineral imbalances), anemia, and SRHP may induce sensory alterations,[1] which alongside uremic oral ulceration, uremic gastroenteritis, and uremic gastric ulceration may reduce food acceptance and appetite. Ideas for increasing food intake include:

- **Palatability enhancement:** Increasing diet palatability by adding water or a renal wet food to

Box 2. Instructions for using dry foods with feeding tubes

If convenient, dry diets intended for dogs with CKD might be used through feeding tubes with diameter of 10 French or more. It is an available and nutritionally appropriate alternative in some situations.

1. Determine the daily food amount by dividing the maintenance energy requirement[19] by the metabolizable energy content (kcal/gram, or kcal/kg divided by 1000) of the selected diet.
2. Use warm water to moisten the food. Add the warm water and wait until the kibbles are soft, then mix in a blender until the slurry is blended and not too viscous to pass through the tube. Add more water if necessary. The goal is to use enough water to soften the food, but too much water will reduce the energy density of the blend, requiring the patient to be fed a higher volume.
3. Remove large particles that could block the tube. Strain or sieve the slurry in a common kitchen sieve. After strained, the mixture is ready to use. If there is concern about the mixture being too thick, try passing it through an unused tube.
4. To avoid overloading the stomach with an excessive volume of food, divide the total volume into at least 6 equal meals. Each meal must be fed at least 2 hours apart.
5. Store the prepared food in a refrigerator for up to 48 hours.
6. Food must be supplied at the approximate temperature of the animal's body. Avoid offering cold or hot food.
7. After each meal, wash the tube by flushing 10 to 15 mL of clean water. Keep the tube's cap closed.
8. Weigh the dog regularly. If the patient gains or loses body weight unintentionally, the feeding amount must be adjusted to support a healthy body weight.

dry diets; adding palatants (while avoiding high phosphorus or high protein foods), such as milk cream, fat sources, or fruits; and warming the diet can stimulate intake. Palatants should be kept to less than 10% of total daily calories. Hand feeding the patient may also be helpful.

- **Appetite stimulants:** Capromorelin, mirtazapine, and cyproheptadine hydrochloride can be used to increase patient appetite,[7] although further research is required to investigate the pharmacokinetics of these appetite stimulants in dogs with CKD.
- **Feeding tubes:** IRIS (2023) recommends considering feeding tube intervention to prevent protein/calorie malnutrition and dehydration in dogs at Stage 4. However, feeding tube intervention must be considered for all patients who do not voluntarily eat after efforts to manage nausea and vomiting, or with the use of palatants or an appetite stimulant. Important benefits of tube feeding include an easier supply of all calories needed, which is sometimes hard to achieve even with appetite stimulants, and a diet with the desired chemical composition (low phosphorus and protein). Tubes can be used not only to provide food but also fluids and medications, helping to maintain or even improve the patient's body weight and hydration status and reducing intravenous or subcutaneous fluid administration needs. Nasoesophageal or nasogastric tubes can be used to provide short-term support depending on patient tolerance, and do not require anesthesia for placement. Esophagostomy tubes should be considered if longer-term support is needed, but they require general anesthesia for placement. If there is high anesthetic risk, a nasoesophageal or nasogastric tube can be temporarily used until patient stabilization is achieved. Larger tubes (> 10 French) used as esophagostomy tubes (or even nasoesophageal/nasogastric tubes in large dogs) allow the use of wet foods or dry kibble blenderized with water into a slurry (**Box 2**), which is very convenient for long-term support.

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PRACTICAL TOOL: DIETARY RECOMMENDATIONS FOR DOGS AND CATS WITH CHRONIC KIDNEY DISEASE

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Selection of a therapeutic kidney diet has been shown to improve quality of life and longevity in both dogs and cats with chronic kidney disease (CKD). While phosphorus restriction remains a cornerstone of nutritional recommendations to slow progression of disease, ideal levels of dietary protein are more nuanced to balance the maintenance of lean body mass while also managing uremia and/or proteinuria. The International Renal Interest Society (IRIS) recommends the following general dietary interventions for patients with CKD:[1]

- Dietary sodium reduction can be considered for patients with systemic hypertension
- Feeding a therapeutic kidney diet to dogs or cats with proteinuria
- Dietary phosphorus restriction to maintain plasma phosphate concentrations starting at IRIS Stage II for both dogs and cats

Although these general recommendations are available, individual dietary recommendations should be made after a complete nutritional assessment of the patient. Care should also be taken to prevent protein and calorie malnutrition through appetite stimulants and assisted feeding modalities (i.e., feeding tube placement) when appropriate.

Table 1. Protein, phosphorus, and sodium requirements and recommendations for dogs and cats with chronic kidney disease

Nutrient (per 100 kcal metabolizable energy)	NRC[2] adult recommended allowance		AAFCO[3] adult minimum requirement		FEDIAF[4] adult minimum recommended level		Suggested nutrient levels for CKD*	
	Dog	Cat	Dog	Cat	Dog[a]	Cat[b]	Dog	Cat
Protein (g)	2.5	5.0	4.5	6.5	4.5	6.25	3.0–6.0	5.75–10.0
Phosphorus (mg) IRIS Stages 1-2 IRIS Stages 3-4	75	64	100	125	100	64	 < 100 < 100	 ≤ 140 < 125
Sodium (mg)	20	17	20	50	25	19	50–100	

[a] Adult based on MER of 110 kcal/kg$^{0.75}$

[b] Adult based on MER of 100 kcal/kg$^{0.67}$

Table 2. Selected nutrients of concern for chronic kidney disease

Nutrient	Considerations for chronic kidney disease
Protein	· Balanced quantity and high quality to maintain lean body mass while managing proteinuria and uremia · Enhance palatability · Reduction in dietary protein intake may be relative to the pet's current protein intake
Phosphorus	· Source of phosphorus, inorganic (highly bioavailable) vs organic (less bioavailable), may influence plasma phosphate concentrations. — FEDIAF advises that additional research is needed to understand the impact of inorganic and organic phosphorus on feline health.[4] · Reduced intake while maintaining an appropriate calcium to phosphorus ratio (ideally between 1:1 and 2:1) · Monitor cats for hypercalcemia while on a phosphorus-restricted diet. If this occurs, consider changing to a less phosphorus-restricted diet.
Sodium	· Avoid excessive restriction (below 40 mg sodium/100 kcal) due to activation of Renin-Angiotensin-Aldosterone System (RAAS) · There is insufficient evidence that reducing dietary sodium will reduce blood pressure in the dog or cat · Therapeutic kidney diets typically avoid high sodium levels
Potassium	· Cats experiencing hypokalemia should be switched to a higher potassium containing diet and/or provided with oral supplementation · Dogs may experience either hypo- or hyperkalemia and dietary intake or supplementation can be modified on an individual basis
EPA (Eicosapentaenoic acid) and DHA (Docosahexaenoic acid)	· Recommended for anti-inflammatory properties · Suggested dosing[5] in the dog is 140 mg/kg$^{0.75}$ EPA+DHA per day (Example for a 10 kg dog: 10 kg$^{0.75}$ x 140 mg/kg$^{0.75}$ = 787 mg EPA+DHA/day) · Suggested dosing in the cat is 200-300 mg EPA+DHA per day · Many therapeutic kidney diets will meet or exceed the suggested dosing making additional supplementation unnecessary · Clinicians can consider dietary concentration first to determine if additional supplementation is necessary
Vitamin D	· Vitamin D supplementation is not currently recommended for CKD patients; however, decreased levels of vitamin D metabolites (i.e., 25-hydroxyvitamin D and 1,25-dihydroxyvitamin D) have been documented in these patients and this is an emerging area of research[6,7] · Care should always be taken with supplementation of Vitamin D because of the potential for excess intake and negative health impacts

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Advancing Science for Pet Health

APPLYING CLINICAL NUTRITION IN PRACTICE

PRACTICAL TOOL: USEFUL CALCULATIONS IN CLINICAL NUTRITION

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Making nutrition recommendations can involve many different calculations, but the most frequently used are those that estimate feeding amounts. To calculate feeding amounts, it is necessary to calculate energy requirements and, in some dogs and cats, target or ideal body weight. Once an animal's maintenance energy requirement—the number of kilocalories needed per day—has been calculated based on current or target weight, the amount of the appropriate diet to feed can be determined with knowledge of the energy density of the chosen diet(s) and other foods included in the nutrition plan.

CALCULATING ENERGY REQUIREMENTS

There are multiple equations that can be used to estimate a dog or cat's energy requirement. The primary equation used in the NRC's Nutrient Requirements of Dogs and Cats is presented below.[1] All equations are starting points and estimate the average energy requirement for an animal of a certain weight. Monitoring the patient to ensure weight maintenance (or weight loss or gain, if desired) is essential as there are animals that need more or less energy than the calculation suggests. In addition, the energy requirements of individual patients with acute or chronic illnesses may vary more significantly from these equations than the requirements of healthy pets.

Resting Energy Requirements (RER)

The RER is the basic amount of energy that is used in a day by a pet remaining at rest. RER, expressed in kilocalories of metabolizable energy (ME) per day, can be estimated with an exponential equation for dogs and cats.[1] As mentioned, there are alternative equations that can be used.

RER (kcal/day) = 70 x (body weight in kg)$^{0.75}$

Current weight is most frequently used in the RER equation, but for some patients, target weight can be used in the equation to provide energy requirements for weight loss or gain.

Maintenance Energy Requirements (MER)

RER is used as a starting point to calculate MER, which more accurately estimates the actual energy requirements of a dog or cat. The daily energy needs of individual dogs and cats are affected by many different variables, including age and life stage, breed, activity level, reproductive status, environment, and health status. For an individual animal, the MER provides an initial estimate of energy requirements, and ongoing assessment of body weight, body condition score (BCS), and other health parameters should then be used to adjust food intake as needed.

To calculate MER, expressed in kilocalories per day, begin with the equation for RER shown above. Use current or target weight as directed below. Then, individual variables must be accounted for by multiplying RER by a specific MER factor.[1-3]

MER (kcal/day) = RER x MER Factor

Commonly used MER factors are listed in **Table 1**. This is not an all-inclusive list—different factors would be required for other life stages, including growth and reproduction, and for sporting dogs. These factors are estimates and patient monitoring is required to ensure weight maintenance, loss, or gain as desired.

ESTIMATING TARGET WEIGHT

It is often necessary to estimate target weight for animals that are not in ideal body condition. It is important to remember that target weight equations provide estimates—the calculations, especially for underweight animals, are not completely accurate for every individual dog or cat due to variations in activity level and other variables. Target weight is based on body condition score and current body weight and is calculated by multiplying the pet's current weight by a target weight factor as described below.

Target weight = current weight x factor based on current body condition score

Table 1. Selected MER factors for dogs and cats

Description of Animal	Current or Target Weight	MER Factor (MER = RER x Factor)
Neutered adult dog	Current	1.6
Intact adult dog	Current	1.8
Obese-prone or inactive adult dog	Current	1.2–1.4
Obese adult dog	Target or current*	1.0
Underweight adult dog	Target	1.4–1.6
Neutered adult cat	Current	1.2
Intact adult cat	Current	1.4
Obese-prone adult cat	Current	1.0
Obese adult cat	Target or current*	0.8
Underweight adult cat	Target	1.2–1.4

* Target weight is often used to determine calorie intake for weight loss; however, current weight can be used if target weight is difficult to determine or if there is concern for drastic calorie restriction leading to nutrient deficiencies or unwanted begging behaviors.

The factors are derived from research indicating that each body condition score point above or below ideal accounts for approximately 10–15% of body weight.[4-6] For overweight patients, the factors (**Table 2**) are described in the 2014 AAHA Weight Management Guidelines.[7]

For underweight patients, the target weight factors are not as well researched or validated, but the ones listed in **Table 3** are calculated similarly to the overweight patient target weight factors.

The target weight factors for both overweight and underweight patients assume the pet's ideal body condition score is 5/9. Some dogs, such as canine athletes and orthopedic patients, may have an ideal BCS of 4/9. If the dog's ideal body condition score is 4/9, the percent overweight increases by 10% and the percent underweight decreases by 10%. To calculate target body weight for a dog with an ideal body condition of 4/9, the target weight factor should be adjusted accordingly. Monitoring during weight gain or weight loss plans is essential.

Table 2. Target weight factors for overweight patients

Body Condition Score	Percent Overweight*	Target Weight Factor (Target weight = current weight x factor)
6/9	10%	0.9
7/9	20%	0.8
8/9	30%	0.7
9/9	40%	0.6

* This is a starting point for calculations. Please keep in mind that it is an estimate. Each patient should be evaluated closely during a weight loss plan to avoid nutrient deficiencies and excessive food restriction.

Table 3. Target weight factors for underweight patients

Body Condition Score	Percent Underweight*	Target Weight Factor (Target weight = current weight x factor)
4/9	10%	1.1
3/9	20%	1.2
2/9	30%	1.3
1/9	40%	1.4

* This is a starting point for calculations. Please keep in mind that it is an estimate. Each patient should be evaluated closely during a weight gain plan.

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PRACTICAL TOOL: DIET HISTORY FORM

PURINA Institute
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Owner's name: _____ Date form completed: _____

Pet's name: _____ Species: _____ Breed: _____

Age: _____ Gender: ☐ Male ☐ Female Neutered/Spayed: ☐ Yes ☐ No

1. What proportion of time does your pet spend indoors or outdoors?

_____ % Indoors _____ % Outdoors When outdoors, is your pet supervised? ☐ Yes ☐ No

2. How active is your pet?

☐ Very active ☐ Moderately active

☐ Not very active ☐ Mostly inactive

3. How would you describe your pet's weight?

☐ Overweight ☐ Ideal weight

☐ Underweight

4. Please list below the brands and product names (if applicable) and the amount of *all* foods, treats, snacks, dental hygiene products, rawhides and any other foods that your pet currently eats, including foods used to administer medications. If homemade diet(s), please provide recipe(s).

Food and Treats (brand, flavor)	Form (dry/wet)	Amount* Per Meal	Frequency	Fed since
*If feeding by volume, what size measuring device do you use?				

5. Do you give your pet any supplements (e.g., vitamins, minerals, probiotics, fish oil, glucosamine, etc.) or other food items not listed above?

☐ Yes ☐ No If yes, please list types and amounts given. _____

6. Have you made any changes to your pet's diet in the last 4 weeks?

☐ Yes ☐ No If yes, please note what change was made and why. _____

7. Do you have any questions about feeding or nutrition for your pet?

For a fillable PDF form, go to: purinainstitute.com/sites/default/files/2021-04/screening-evaluation.pdf

RT/CRCT

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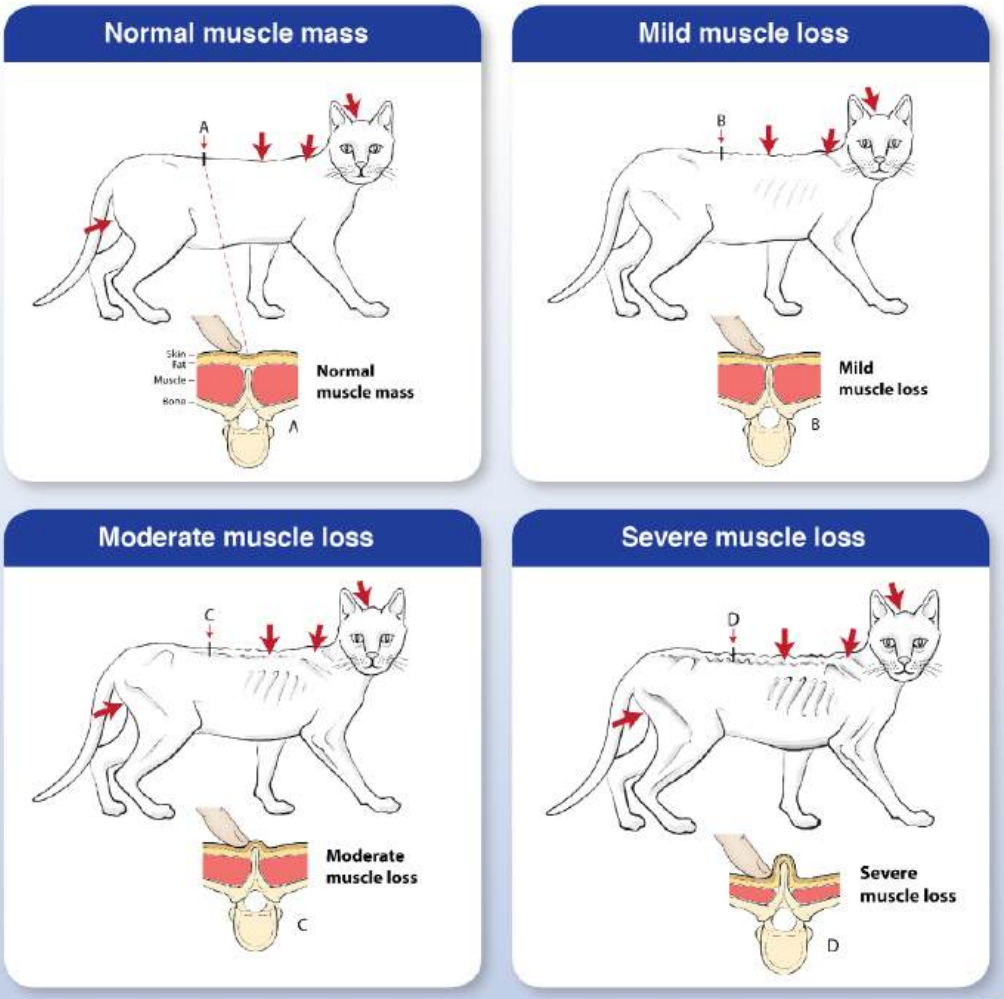
Muscle Condition Score

Muscle condition score is assessed by visualization and palpation of the spine, scapulae, skull, and wings of the ilia. Muscle loss is typically first noted in the epaxial muscles on each side of the spine; muscle loss at other sites can be more variable. Muscle condition score is graded as normal, mild loss, moderate loss, or severe loss. Note that animals can have significant muscle loss even if they are overweight (body condition score > 5/9). Conversely, animals can have a low body condition score (< 4/9) but have minimal muscle loss. Therefore, assessing both body condition score and muscle condition score on every animal at every visit is important. Palpation is especially important with mild muscle loss and in animals that are overweight. An example of each score is shown below.



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Muscle Condition Score

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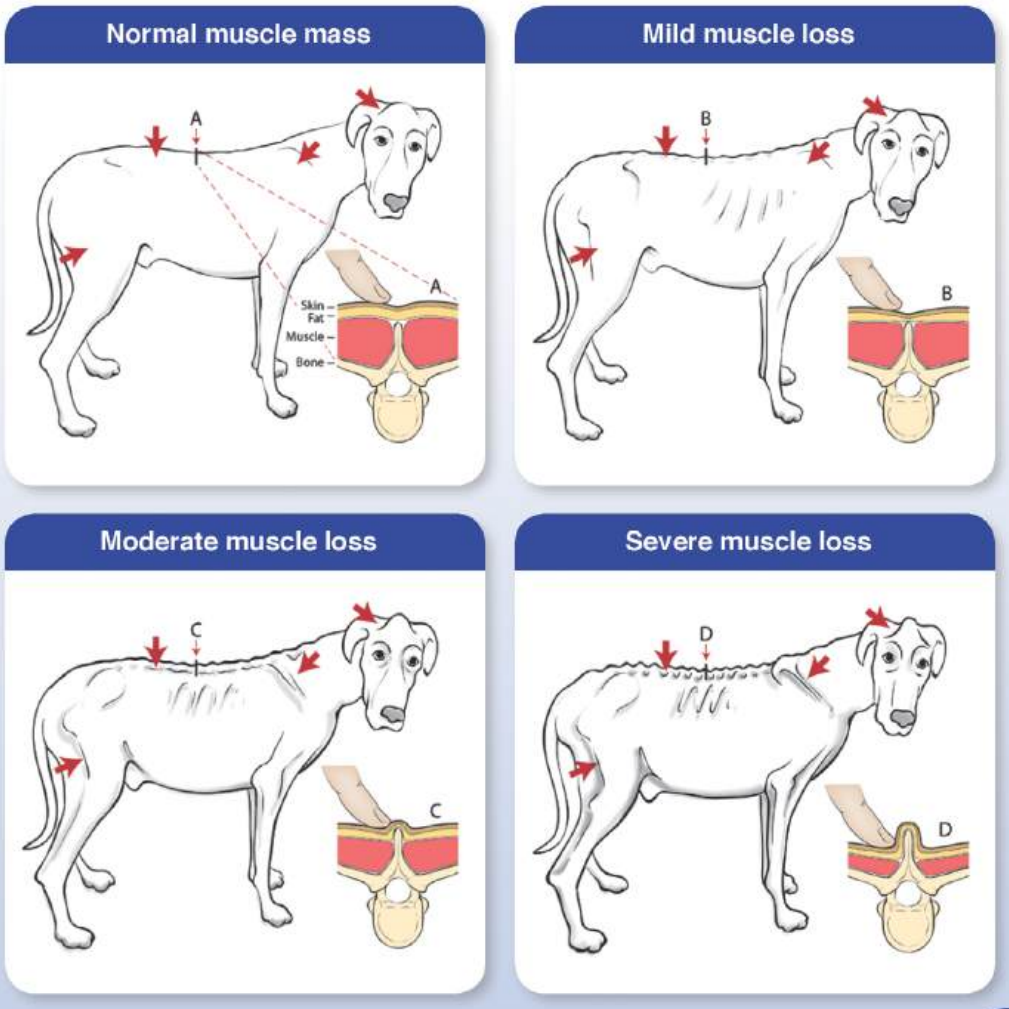

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Updated on 10 March 2021

WSAVA Global Nutrition Committee: Guidelines on Selecting Pet Foods

Pet food labels include a lot of required and useful information for veterinary teams and pet owners. They may also include marketing images and phrases that are designed to promote product sales rather than relay nutritional information. This means that some of the information, including unregulated terms such as 'holistic' or 'premium', is of little practical value for nutritional assessment. The veterinary team has a vital role in helping pet owners make informed decisions on the optimal diet for their dog or cat.

What to look for in a brand

1. Do they employ a Nutritionist?

- Appropriate qualifications are either a PhD in Animal Nutrition or Board Certification by the American College of Veterinary Nutrition (ACVN) or the European College of Veterinary Comparative Nutrition (ECVCN).
- What are the Nutritionist's name, qualifications and employment status? Consultants may have limited influence compared to a staff Nutritionist.

2. Who formulates the diet?

- Is the recipe developed by an experienced pet food formulator (MS or PhD in Animal Nutrition), a veterinarian, or a pet owner/breeder/trainer?
- Recipe development is a complex process requiring knowledge of nutrition, raw materials, and processing not taught in veterinary school programs.
- Trained and experienced formulators may have a degree (MS/PhD) in food science and technology to help guide ingredient selection and nutrient levels for health or disease management.
- An individual with Board Certification by ACVN or ECVCN may also be cross-trained in pet food formulation or work in collaboration with experienced pet food formulators to help guide ingredient selection and nutrient levels.

3. What is the quality control process for ingredients and finished products?

- Diets formulated to meet Association of American Feed Control Officials (AAFCO) or European Pet Food Industry Federation (FEDIAF) guidelines should meet their nutrient profiles. Does the diet meet the profile based on analysis using a nutrient database or on chemical analysis of the finished product?
- Manufacturers and pet food providers should have adequate quality control to ensure companion animal and owner safety. This should include ingredient (food and supplement) validation, final diet nutrient analysis, toxicology, bacteriology, and packaging/shelf-life screenings prior to, during, and after manufacturing.

4. What kind of product research or nutrition studies have been conducted? Is it published in peer-reviewed journals?

- Pet food companies are not required to conduct or sponsor nutritional research in order to produce and sell a food, but when they do, it indicates a commitment to animal health and wellness.

What to look for on a label

1. Nutrition Adequacy Statement?

- Is it a complete diet? Foods should be labeled to indicate if they provide a "complete" diet with all required nutrients. The label might also specify if this was determined via life stage feeding trials vs formulation to meet requirements. Those labeled as intended for "short-term", "intermittent", or "complementary" feeding should only be fed as a small portion of the diet (10% or less), or under veterinarian supervision if feeding a therapeutic diet.
- Does the food match the nutritional needs of the individual dog or cat? AAFCO and FEDIAF provide pet food manufacturers with recommended nutrient levels for different life-stages (reproduction, growth, and adult) for healthy dogs or cats. Diets labeled "for all life-stages" are formulated for reproduction and growth.

2. How many calories per gram or serving of food?

- Obesity prevalence is increasing in pets in many areas of the world. Having access to accurate pet food caloric content can help prevent unintended overfeeding. Calorie information is only required on pet food labels in the US. Where it is not provided on the label it should be available by contacting the manufacturer or calculating from label nutrient analysis.

3. Does the company provide immediate contact information such as a phone number or email address?

- Company representatives should be easily accessible for additional questions, such as the level of specific nutrients not on the label. Pet food companies should be able to provide an "average" or "typical" analysis for all essential nutrients in their food.

4. Who makes the food?

- Companies may make their own food (i.e.,"Made by") or use a third- party manufacturer (i.e.,"Made for" or "Distributed by").

If the manufacturer cannot or will not provide any of this information, veterinarians and owners should be cautious about feeding that brand.

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NUTRITIONAL ASSESSMENT

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KEY TAKEAWAYS

- Nutritional assessment is vital for maintaining the health and welfare of dogs and cats as well as for disease management.
- The screening nutritional assessment, comprised of diet history, body weight, body condition score, muscle condition score, skin and coat health examination, and dental examination, adds little time and no cost to a veterinary consultation, and provides great benefits for pets and for their owners.
- An extended nutritional examination should be performed when risk factors are found or suspected.

INTRODUCTION

Nutritional assessments are critical for maintaining pets' health and their optimal response to disease and injury. The World Small Animal Veterinary Association (WSAVA) has established guidelines for nutritional assessment as the 5th vital assessment incorporated into the standard anamnesis and physical examination.[1] The nutritional assessment requires little time and no cost, is greatly beneficial for pets, and enhances the bond between owners and the veterinary team.

The standardized assessments include:

1. temperature
2. pulse
3. respiration
4. pain assessment
5. nutritional assessment

COMPONENTS OF A NUTRITIONAL ASSESSMENT

Nutritional assessment includes consideration of animal-specific factors, diet-specific factors, feeding management, and environmental factors.[1]

Animal-specific factors include age, life stage, activity, and nutrient-sensitive disorders requiring specific dietary management (e.g., chronic kidney disease, obesity).

Diet-specific factors include the safety and appropriateness of the diet and include nutrient imbalances, spoilage, and contamination. Feeding an unbalanced homemade or poor-quality commercial diet are within this part of the assessment.

Feeding and management factors include the frequency, timing, location, and method of feeding. Feeding management includes over- or under-feeding, treats/snacks/human foods, scavenging, and hunting. Environmental factors include the pet's housing, presence of other animals, access to the outdoors, and environmental enrichment.

Owner factors and the owner's relationship with their pet should also be taken into consideration (**Figure 1**). Good communication with owners is vital and is addressed elsewhere.

Nutritional assessment is a two-part process comprising a screening evaluation and, when needed, an extended evaluation (**Figure 2**).[1]

Screening Evaluation

The screening evaluation should be part of routine history taking and physical examination at every veterinary visit. It includes the diet history, body weight, body condition score (BCS), muscle condition score (MCS), and evaluation of the coat and oral health.

Diet history, body condition score, and muscle condition score are covered elsewhere.

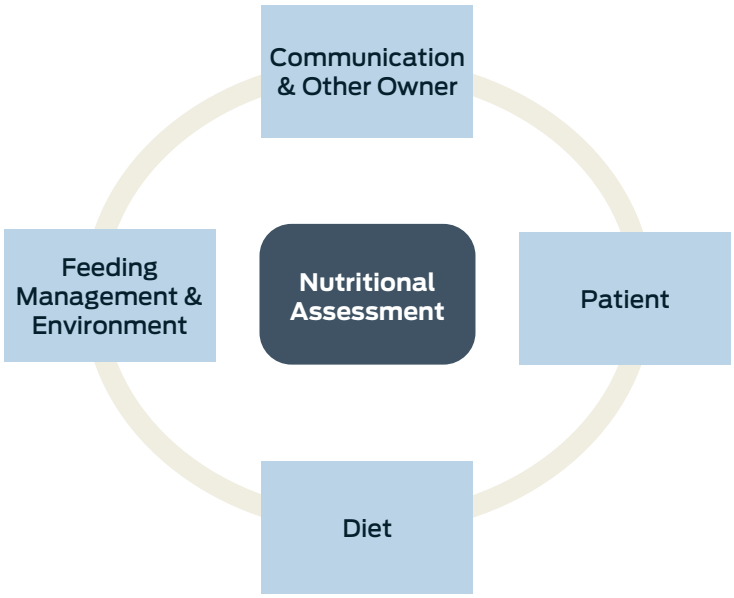
Body condition scores using a 9-point scale show good repeatability.[2,3] Lower BCS numbers indicate underweight and higher numbers indicate overweight/obesity. For dogs, a BCS of 4/9 to 5/9 is ideal. A score of 4/9 would be appropriate for typically leaner breeds (e.g., Greyhounds) or working dogs. For cats, a BCS of 5/9 is generally considered ideal, with a BCS of 6/9 being ideal for some cats.[4] Middle-aged or senior cats and those with chronic disease conditions (e.g., kidney or heart disease) may have better survival times with a BCS of 6/9 rather than < 5/9 or > 7/9.[4–6]

Body condition charts include profile and "top-down" pictures with written descriptions. Body condition is determined using a combination of visual appearance, e.g., if there is a waist apparent looking down on the pet and an abdominal tuck visible from the side profile, and palpation of the fat cover over the ribs. The owner should be shown how to palpate their pet, placing their hands gently in a flat position over the pet's ribs (**Figure 3**).

The BCS evaluates body fat; however, it is possible for a pet to have excess fat but still have muscle loss (e.g., diabetic cats and other ill or aged pets). Acute or chronic disease can cause loss of muscle mass disproportionate to the loss of fat due to cytokine and neurohormonal effects on metabolism.[7] Muscle mass scoring systems are based on palpation of skeletal muscle over the skull, scapulae, spine, and pelvis[1]. Animals are scored as having normal, mild, moderate, or severe muscle wasting.

Every pet owner should leave the hospital or appointment with a written dietary recommendation

Figure 1. Screening evaluation factors including owner communication



Patient factors include age, life stage, activity, and nutrient-sensitive disorders requiring specific dietary management.

Diet factors include safety and appropriateness of the diet and include nutrient imbalances, spoilage, and contamination.

Feeding management and environmental factors include feeding frequency, timing, location, and method of feeding; over- or under-feeding; extra foods; housing; presence of other animals; access to the outdoors; and environmental enrichment.

Communication and other owner factors include the owners' lifestyle (e.g., work and family commitments), members of the household, beliefs about pet food and feeding, relationship with the pet, and their communication styles with the veterinary team.

Figure 2. Flow chart for screening and extended nutritional assessments

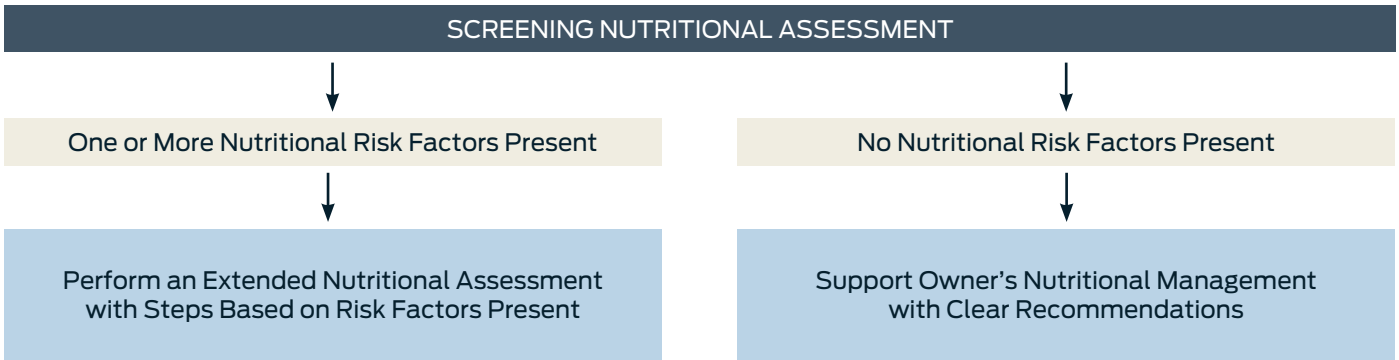


Figure 3. Demonstration of palpation of the ribs of a cat for a body condition score

on a discharge sheet along with any other instructions, e.g., for medication. If no change is recommended, the owners should be advised that the current diet and management are appropriate.

Extended Evaluation

An extended evaluation should be performed if nutrition-related risk factors are found or suspected on the screening evaluation or medical assessment. A checklist for indications for an extended evaluation is available from the WSAVA website.[8] The items on the checklist are discussed below.

RISK FACTORS INDICATING EXTENDED EVALUATION

Animal risk factors indicating an extended evaluation include over or under ideal BCS, unintentional weight gain or loss, decreased muscle condition, changes in food intake or feeding behavior, changes in the coat or skin (e.g., dryness or alopecia), altered gastrointestinal function (e.g., vomiting, diarrhea, nausea, flatulence, constipation), dental abnormalities or disease, and new or previous or ongoing medical conditions/disease. Growing puppies and kittens and queens or bitches in gestation or lactation may also require an extended evaluation.

Abnormalities in the serum chemistry profile (e.g., high or low glucose, albumin, total protein, electrolytes, urea, creatinine, or thyroid hormone), urinalysis, fecal examination, or other diagnostic tests should also trigger an extended evaluation and medical diagnostic workup.

Dietary risk factors include medications and/or supplements, unconventional diets (e.g., raw, homemade, vegetarian, grain free), a diet unfamiliar to the clinician, hunting or scavenging, begging, extra foods (e.g., snacks, treats, human foods) comprising more than 10% of total calories, and any concerns with food safety.

Feeding management concerns include multiple pet households (e.g., potential competition for or guarding of food), inappropriate location of food and water bowls, inadequate feeding frequency, decreased or increased spontaneous activity level, environmental stressors, and inadequate or inappropriate housing.

EXTENDED NUTRITIONAL ASSESSMENT

The extended evaluation depends upon what risk factors are suspected or found.

Diet factors in an extended evaluation may include caloric density, food ingredients, and supplements. Treats, human foods, food given to administer medications, and successful hunting or scavenging should be evaluated for their effect on diet balance and caloric intake. If disease conditions exist which may be due to contamination of the food, food testing should be performed. Raw foods carry a higher risk of bacterial contamination than those that are cooked.

Diets should be appropriate for the pet's nutritional life stage (i.e., growth, adult, reproduction). There is no unique life stage nutritional profile for senior or geriatric cats or dogs. They are included as "adults," but they should be fed as individuals as no single type of diet is suitable for all older pets.

Diets should be formulated to meet FEDIAF,[9] AAFCO,[10] or NRC[11] nutrient requirements. Commercial pet food companies usually use FEDIAF or AAFCO requirements

as they are adapted for use in commercial diets. Ideally, appropriate feeding trials of commercial diets will have been performed to demonstrate they are nutritionally replete. The quality control protocols, reputation, and research of the company are also important factors.

Homemade diets should be checked to determine if they are complete and balanced. The owner may need to be referred to a board-certified veterinary nutritionist for homemade diet analysis or formulation.

COMMUNICATION TIP

"Small animal clinics have reported an improvement in consistency of the total examination process, more discussion on nutrition, and better wellness care after implementation of nutritional assessments."

Therapeutic diets may be indicated, and the use of the correct diet should be assessed. Not all patients with a disease (e.g., hepatic, renal, cardiac disease) need to be on a commercial therapeutic diet labeled for that disease. A concurrent disease may take precedence over the one for which the diet is being fed, or the diet may not be appropriate for that individual pet. For example, for pets in early stages of chronic kidney disease, an early renal diet may be more appropriate than a severely protein-restricted diet.[12,13]

Extended evaluation feeding management factors include multiple pets, resulting in either competition or pets receiving an inappropriate diet (e.g., all household pets inappropriately fed a renal diet meant for one pet, puppies fed adult foods). Environmental factors include the pet's activities; living indoors, outdoors, or both; availability and accessibility of clean water (e.g., an arthritic dog unable to climb stairs to the bowl); and, for inside cats, access to a clean litter box (e.g., a cat guarding the box or infrequent litter box cleaning). Stress due to other animals within the household or outside the house, negative interactions with family members, or being left alone for long periods of time have an impact on the pet's health. Pets may show competitive eating, coprophagy, or obesity due to environmental factors. For example, indoor confinement and physical inactivity are risk factors for overweight in cats whereas feeding balls or interactive toys increase activity and decrease food intake.

HOW TO INCORPORATE A NUTRITIONAL ASSESSMENT INTO PATIENT APPOINTMENTS AND EXAMINATIONS

Nutrition and nutritional assessment ideally should include all of the health care team, including receptionists, veterinary technicians/nurses, and care assistants as well as veterinarians. An awareness of the clients' desires to have nutrition information from the veterinary team as well as the importance of nutrition for pet health should be discussed at a team meeting. Veterinary team members sometimes feel their nutrition knowledge is inadequate to provide guidance to pet owners. The WSAVA Global Nutrition Toolkit and WSAVA Academy Nutrition Modules can provide the education and confidence to incorporate nutrition into clinic consultations.[14]

Sending diet history forms to owners prior to the consultation or having them come to the clinic a bit early to fill them out saves time in the examination room. They can then be screened for any dietary risk factors that need to be discussed with the client.

Creating templates in the objective part of SOAP (subjective, objective, assessment, plan) examination record provides a stimulus for including and recording BCS and MCS as well as body weight, and dermatological and dental assessments.[15] These should either have no default or default to zero if not performed rather than to normal or good. A scan of the record then shows if the assessment has been omitted. Charts for BCS and MCS should be available in the records and/or easily seen in the examination room. Performing a BCS, MCS, coat, and dental assessment adds very little time to the physical examination process.

The assessment part of the SOAP record would include nutritional assessment of the current diet. The plan includes a recommendation to continue with the current diet and management of any changes recommended. If risk factors are found on the screening assessment, another appointment for an extended assessment may be beneficial.

After nutritional assessment has been incorporated into the clinic, follow-up reviews will determine if the staff needs any changes to help implement the program. Small animal clinics have reported an improvement in consistency of the total examination process, more discussion on nutrition, and better wellness care after implementation of nutritional assessments.[15]

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OBTAINING A COMPREHENSIVE NUTRITIONAL HISTORY

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KEY TAKEAWAYS

- Obtaining a comprehensive nutritional history is the foundation for performing a nutritional assessment and should be completed as part of every veterinary assessment.
- A comprehensive nutritional history is comprised of 1) patient factors, 2) diet factors, 3) environmental factors, and 4) human factors.
- When obtaining a nutritional history, the veterinary healthcare team should utilize a combination of verbal and written communication strategies, such as open-ended inquiries and nutritional history forms.

IMPORTANCE OF A COMPREHENSIVE NUTRITIONAL HISTORY

Obtaining a comprehensive nutritional history is fundamental to assessing patient wellness. According to the World Small Animal Veterinary Association (WSAVA), the "five vital assessments" should be performed at each veterinary assessment and include 1) temperature, 2) heart rate, 3) respiratory rate, 4) pain assessment, and 5) nutritional assessment.[1] Over a decade ago, the WSAVA Global Nutrition Committee published Nutritional Assessment Guidelines that highlight the nutritional assessment as the "fifth vital assessment," of which obtaining a comprehensive nutritional history is a key component.[1]

DEVELOPMENTS IN OBTAINING A COMPREHENSIVE NUTRITIONAL HISTORY

Performing a nutritional assessment is an iterative process that begins by screening each patient for nutritional risk factors, which includes the patient's nutritional history, medical history, and physical examination findings.[1,2] The comprehensive nutritional history is comprised of a detailed evaluation of 1) patient factors, 2) diet factors, 3) environmental factors, and 4) human factors.[2] Previously, the recommendation of the American College of Veterinary Nutrition was to focus on "the circle of nutrition" (see **Figure 1**), which lacked specific emphasis on human factors.[3] Given the role humans play in provision of nutrition to domesticated cats and dogs, adding a fourth category to focus solely on "human factors" in the 2021 American Animal Hospital Association (AAHA) Nutrition and Weight Management Guidelines for Dogs and Cats was an important step.[2]

A SYSTEMATIC APPROACH: THE FOUR FACTORS

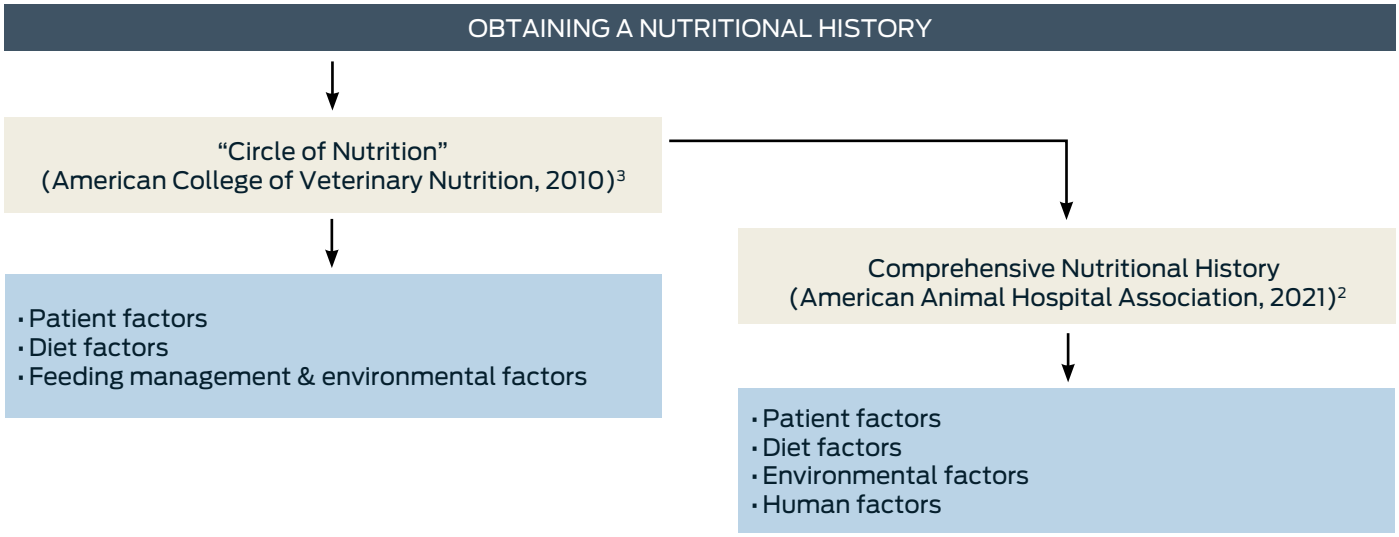
The four factors of the comprehensive nutritional history serve as the framework for the systematic approach to gathering this pertinent information. Detailed examples of information to be gathered for each of the factors is shown in **Box 1**.[1-5]

OBTAINING A COMPREHENSIVE NUTRITIONAL HISTORY

Communication strategies are not only important when it comes to the efficiency of obtaining a nutritional history, but also to ensure the information is comprehensive. An efficient approach involves a combination of both verbal (incorporating interpretation of non-verbal cues from pet owners) and written communication strategies by the veterinary healthcare team.[6] Gathering a comprehensive nutritional history is a process that can build rapport and trust with pet owners through openness and empathy on the part of the veterinary healthcare team.

For efficiency, the process should begin with having the main person caring for the patient complete a written nutritional history form at home and then

Figure 1. Development of factors included in obtaining a comprehensive nutritional history. Both sets of factors are meant to be iterative processes. In other words, the factors are assessed and then reassessed as needed.



either bringing/emailing the form to the clinic prior to the patient's scheduled assessment (see **Box 2** for examples).[6] Collecting this detailed information requires sufficient time for it to be useful to the veterinary healthcare team, so forms should be provided at least 1 week in advance of scheduled assessments. Providing this form in advance improves the completeness of the nutritional history, especially if the main person caring for the patient cannot attend the veterinary assessment. Additionally, information gathered on the form assists with efficient medical record keeping and provides a starting point for the veterinary healthcare team to ask clarifying questions during the veterinary assessment. This written form does not replace verbal communication, which is essential for building rapport and trust with pet owners.

To initiate the verbal component of gathering a comprehensive nutritional history, gauge the owner's willingness to discuss their pet's nutritional history by asking for example, ***"As part of assessing your cat's overall wellness I would like to discuss her nutrition and activity. Would it be alright if we go over this in detail?"***[2] Pet owners are usually receptive when asked for permission.[2] If a pet owner is apprehensive, as demonstrated either via verbal or non-verbal cues, use this as an opportunity to demonstrate respect by offering to set up a follow up consultation at a later date/time. If the pet owner outright declines, move on with the remainder of the consultation given this pet owner is not likely to be responsive to nutrition discussions at this time.[2]

Open-ended inquiries should initially be utilized to allow for more efficient and complete information gathering than starting with closed-ended questions that often prompt one-word answers.[2,6,7,8] The use of open-ended inquiries has consistently demonstrated that a more comprehensive nutritional history is obtained when compared with use of "what-prefaced" questions, such as "What food are you feeding your dog?"[7] Utilizing "what-prefaced" questions often yields brief answers that tend to be restricted to only the commercial brand and subtype (i.e., kitten food) as responses.[8] Comparatively, asking, ***"Tell me everything your dog eats throughout a day, starting from first thing in the morning right through to the end of the day"*** is less restrictive, and provides a clinician with more information.[2,7] After initially using open-ended inquiries, funnel down to more specific questions, including closed-ended questions, to clarify any missing information.[2,6] For further examples, please review: Gathering a Comprehensive Nutrition History (aaha.org).[2]

After reviewing the patient's comprehensive nutritional history, the final step is to check in with the pet owner to determine if they have any concerns regarding their pet's nutrition.[2,6] For example, ***"Now that we have reviewed your pet's history, please tell me about any concerns you have regarding his nutrition."*** Clarifying any concerns the pet owner expresses through active listening (i.e., making eye contact and not rushing the client) and paraphrasing the concerns expressed are critical steps to ensure the pet owner feels heard.[2,6]

Box 1. Detailed information to be gathered for each patient using the four factors of the comprehensive nutritional history

FACTOR 1 – PATIENT FACTORS:

- Patient signalment:
  - Age (i.e., growth, adult maintenance, senior, geriatric)
  - Breed and consideration of known breed predispositions (e.g., obesity in Labrador Retrievers)
  - Sex (i.e., intact, spayed, neutered)
- Physical examination:
  - Current weight and weight trends over time (i.e., increasing, stable, or decreasing weight over time)
  - Body condition score (BCS) using the 9-point scale[5]
  - Muscle condition score using normal muscling, mild muscle loss, moderate muscle loss, or severe muscle loss[5]
- Medical history:
  - Patient's past and current medical conditions, including if the patient is over-conditioned (BCS > 5/9) or under-conditioned (BCS < 4/9 for dogs, < 5/9 for cats)
  - Current prescribed medications including monthly preventatives
  - Current recommended supplements (e.g., probiotics, fat supplements, joint support supplements, vitamin and mineral supplements, etc.)
  - Daily appetite (e.g., polyphagic, hyporexic, anorexic) and any begging behaviors (i.e., begging for food in the middle of the night)
  - Fecal scores using the 7-point Purina Fecal Scoring System, number of bowel movements daily, and any changes
  - Other gastrointestinal signs including nausea, vomiting including trichobezoars, regurgitation, eructation, borborygmi, flatulence, anal gland issues, etc.
    - If vomiting or regurgitation is present determine the time of day in relation to timing of meals (i.e., before, during, immediately after, several hours after), any known triggers, the appearance, etc.
  - Issues with dietary indiscretion or pica (e.g., grass/leaves/sticks, another pet's food, garbage/compost, pieces of bone/toys/socks, etc.)
  - Urination frequency and volume (e.g., polyuria, oliguria, etc.) and any changes or concerns (e.g., hematuria, dysuria, etc.)

FACTOR 2 – DIET FACTORS:

- Determine the base foods the patient is eating or being offered:
  - Commercial base food examples:
    - Shelf-stable dry (e.g., extruded, or baked kibbles, semi-moist foods)
    - Shelf-stable wet (e.g., cans, pouches, etc.)
    - Shelf-stable mixers (i.e., cooked animal proteins and oils/fats are typically added to these products in an attempt to make a balanced food)
    - Perishable cooked (e.g., bowls, pouches, tubes, etc. that require storage in the freezer/refrigerator)
    - Perishable raw (uncooked/lightly cooked) (e.g., pouches, tubes, bags, etc. that require storage in the freezer/refrigerator and may have undergone high pressure pasteurization, had bacteriophages added, or been washed in acid (e.g., peracetic acid), etc. for pathogen control)

Box 1 continued

- Homemade base foods (either cooked/uncooked):
  - No recipe is being followed
  - Recipe is being followed from an unknown source
  - Recipe is being followed from a source without the training required to balance the recipe
  - Recipe is being followed and was formulated by a MSc or PhD Animal Nutritionist with training in balancing diets for cats and dogs
  - Recipe is being followed and was formulated by a Board-Certified Veterinary Nutritionist® with training in balancing diets for cats and dogs

- For all commercial base foods determine the following for the past 12 months:
  - Brand and full product name (e.g., [Brand name] Complete Adult Dry Dog Food with Real Beef)
    - Ideally have the owner provide the weblink to the product for clarity
  - Amount and frequency (e.g., 2 cups twice daily, 126 grams daily over 3 meals)
    - If a volumetric measuring device (e.g., measuring cup, scoop, etc.) is being used, have the owner provide a picture for clarity
  - Fed since (e.g., June 2019)
- For all homemade base foods (either cooked/uncooked) determine the following for the past 12 months:
  - Specific ingredients being fed and how they are prepared (e.g., pan-browned, 95% lean/5% fat ground turkey or boiled long-grain brown rice)
  - Amounts being included (e.g., ½ cup once daily, 85 grams twice daily)
  - Supplements being added (e.g., vitamin and mineral supplements, salt, etc.)
  - Fed since (e.g., June 2019)
- For all commercial treats (e.g., biscuits, chews, bones, pill administration treats, etc.) determine the following for the past 12 months:
  - Brand and full product name (e.g., [Brand name] Chicken Flavor Moist Treats)
    - Ideally have the owner provide the weblink to the product for clarity
  - Amount and frequency (e.g., 2–3 treats twice daily)
  - Fed since (e.g., June 2019)
- For all homemade treats (either cooked/uncooked) determine the following for the past 12 months:
  - Specific ingredients being fed and how they are prepared (e.g., roasted boneless skinless chicken breast or raw baby carrots)
  - Amount and frequency (e.g., 3 baby carrots daily)
  - Fed since (e.g., June 2019)
- Patient preferences:
  - Determine what foods/treats the patient prefers
  - Determine what foods/treats the patient does not readily consume or does not tolerate

FACTOR 3 – ENVIRONMENTAL FACTORS:

- Day in the life of the patient:
  - Determine the patient's daily schedule from the time they wake up until the time they go to bed (i.e., Please tell me about a day in the life of your pet)

Box 1 continued

- – Where does patient spend most of their time (e.g., indoors, outdoors)? If outdoors, how is the patient secured (e.g., fenced yard, enclosed catio, etc.)?

- Other pets in the home:
  - – Are there other pets in home? If so, determine the specific pets and types of interactions, especially those that impact food intake or feeding management (e.g., one parrot that drops food frequently for the patient)
  - – Does the patient have access to another pet's food?
  - – Does the patient eat out of another pet's bowl/dish/feeder?
  - – Does the patient have access to trash/compost/dishwasher?
  - – Is there competition for food between pets?
- Activity:
  - – Determine the patient's daily activity (e.g., 1 hour of walking per day, 5 minutes of chasing the ball in the yard, etc.)
  - – Determine the type of work or exercise (if any) patient does on average week (e.g., agility training 2 days per week for 1 hour each)
  - – Determine any routine outings (if any) that involve activity (e.g., doggie daycare 3 days per week with playgroups for several hours each day)

FACTOR 4 – HUMAN FACTORS:

- Physical Examination:
  - – Does the owner consider their pet to be over-conditioned, ideal, or under-conditioned? Does this match the veterinary healthcare team's assessment?
  - – Does the owner have any concerns regarding their pet's physical condition (i.e., lameness, dry skin/coat, bad breath, etc.)?
- Medical History:
  - – What past/current medical conditions is the owner most concerned about?
  - – Are prescribed medications being given properly by the owner?
  - – Are recommended supplements being given properly by the owner?
- Nutritional History:
  - – What are the owner's primary concerns related to nutrition?
- Human Environment:
  - – Who feeds the patient meals? Is there more than one person?
  - – Who gives the patient treats? Is there more than one person?(e.g., children in the home dropping food from highchairs for the patient to eat)
  - – How many adults and children are in the home? (e.g., 1 adult and 2 children ages 3 years and 5 years)
  - – Are there any challenges in the home related to feeding the patient? (e.g., grandmother with dementia that forgets how often she is feeding the patient)
  - – Is there any care provided by people outside the home? (e.g., dog walker)

COMMUNICATION TIP

"Open-ended inquiries should initially be utilized to allow for more efficient and complete information gathering than starting with closed-ended questions that often prompt one-word answers."

Lastly, obtaining a comprehensive nutritional history takes time. Booking follow-up telehealth appointments via phone or videoconferencing platforms, or telling clients to expect a longer appointment and scheduling time for the comprehensive nutritional history, helps reduce the tendency to rush pet owners during nutrition conversations and ensures the veterinary healthcare team stays on schedule.

Box 2. Nutritional history form examples

- American College of Veterinary Internal Medicine (Nutrition):[9] https://bit.ly/Nutrition-diet-form
- Purina Institute CentreSquare:[10] https://www.purinainstitute.com/sites/default/files/2021-04/screening-evaluation.pdf or here
- World Small Animal Veterinary Association Global Nutrition Committee Nutrition:[11] https://wsava.org/wp-content/uploads/2020/01/Diet-History-Form.pdf

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COMMUNICATING WITH CLIENTS ABOUT NUTRITION TO PROMOTE COMPLIANCE

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KEY TAKEAWAYS

- A collaborative client-centered relationship with the veterinary health care team (VHCT) positively influences treatment outcomes.
- Intentional and empathetic communication employed by the VHCT engages and empowers the pet owner. By listening to what clients have to say and asking nonjudgmental questions with a focus on emotional needs, shared decision-making is improved.
- By implementing knowledge of behavioral change, the veterinary health care team can achieve the goal of helping the client understand their pet's condition and treatment options, and ensure they involve the client in a mutually agreed-upon care plan and ongoing assessment that best fits the family and pet.

INTRODUCTION

Successfully helping pet owners understand and follow food and feeding management recommendations remains challenging for many veterinary health care teams. Despite pet owners wanting specific nutrition recommendations from their veterinary health care team, many pet owners report that they do not receive this information. Despite efforts by the VHCT to provide specific nutrition recommendations, they still face barriers to client compliance to the nutritional recommendations given for their patients. Many factors impact the successful compliance of a recommended nutritional care plan, such as a lack of owner understanding, lack of trust and rapport with the veterinarian, preconceived ideas and misunderstandings about pet food, and, potentially, resistance to change. Excellent communication skills by the VHCT partnered with an understanding of models of behavior change can be used to put strategies in place to improve client compliance to nutritional therapy.

TERMINOLOGY

In human health care, the following definitions are suggested. *Compliance* refers to a passive process whereby the patient has their prescribed therapy enforced. *Adherence* also refers to a passive process in which an informed patient will stick to the prescribed treatment. *Concordance* is a process of informed communication between the patient and their health care team, leading to an agreed-upon treatment and ongoing assessment plan.[1] In veterinary medicine, these terms may be used interchangeably, and the differences not universally understood. Concordance captures the standard of best practice, with the VHCT and an empowered pet owner partnering in shared decision-making to provide the best treatment plan for the pet. Because concordance is not a commonly used term in veterinary practice, and the ultimate goal is for the pet to receive the most appropriate treatment plan, the term "pet owner compliance" will be used throughout and defined as the implementation of a treatment as agreed upon and planned.[2]

CORE COMMUNICATION SKILLS BUILD COLLABORATIVE RELATIONSHIPS WITH CLIENTS

The relationship between the VHCT and the pet owner has a great impact on client compliance. Studies in human health care suggest relationship-centered recommendations have better levels of clinician and patient satisfaction as well as improved patient outcomes.[3] Shaw[4] described four core communication skills that promote a positive veterinarian-client-patient relationship: 1) open-ended questions, 2) reflective listening, 3) nonverbal communication, and 4) empathy. Although not intuitive, open-ended

inquiry, such as "Tell me everything your pet eats in a day," can be used to efficiently gather crucial information as well as build a trusting relationship with the client. Using nonjudgmental phrases such as "Tell me about," "Describe for me," or "What type of treats do they enjoy?" to collect diet history information can elicit the owner's perspective as well as information that will help develop a nutritional plan. After asking open-ended questions, summarizing or clarifying information with reflective listening can let owners know they are being listened to, but also can redirect owners back to the concern at hand if they get lost in details. When speaking with clients, particularly about a controversial and emotional topic such as nutrition, nonverbal communication is critical to be aware of. If the discussion is positive but the pet owner is not maintaining eye contact, frowning, or crossing their arms, then there are mixed messages that should be explored further to ensure clear communication. Lastly, empathy with a focus on education in lieu of judgment on any previous decisions a pet owner may have made can greatly build trust in the exam room. Employing these four core communication strategies while discussing nutrition with clients can help owners feel valued and respected, which can lead to increased trust with the VHCT and improved outcomes for patients.

Research[5] suggests that communication skills and the approach taken by the VHCT can positively impact a client's engagement in shared decision-making in the care of their pet as well as the client's satisfaction in the care they receive. **Figure 1** illustrates how communication can influence shared decision-making with a pet owner.

Central to veterinary practice and implementing a successful care plan is changing a client's behavior.[6] In the case of clinical nutrition, the veterinarian must engage with a client to incorporate recommendations for foods and feeding management to proactively promote health or to begin a therapeutic dietary plan. This often involves the selection of a new food or treats or a change in feeding management. Research indicates practitioner communication skills to create a relationship-centered approach can improve client motivation and patient behavioral outcomes.[7,8]

APPLY MODELS OF BEHAVIOR CHANGE TO IMPROVE COMPLIANCE

There are many models of behavior and behavioral change. Understanding two models in particular may provide practical strategies and ways to guide communication to successfully integrate nutritional

Figure 1. A shared decision-making plan[5]

UNDERSTAND THE CLIENT	PROVIDE INFORMATION TAILORED TO THE CLIENT	HELP THE CLIENT MAKE THEIR DECISION
▼	▼	▼
• Invite the client to partner in their pet's care Example: Ask "What do you hope we can do together today?"	• Use language and terminology that the specific client can understand and benefit from	• If possible, provide options for the client that they can use to make an informed decision with your guidance and recommendation
• Gain understanding of where the client is with their knowledge of the situation Example: Ask "What is your understanding of Sadie's kidney disease?	• Check for understanding and invite questions to clarify	• Make sure the client understands that they will take part in the decision-making process
• Appreciate the client's body language and other nonverbal communication to better understand the client's worries, or willingness and readiness	• Provide relevant references such as reputable websites and other resources	• Follow up and be available to answer questions or troubleshoot difficulties implementing the plan at home, so clients do not feel "they decided alone"
	• Utilize the VHCT to reinforce information	

Table 1. Examples to improve capability, opportunity, or motivation to effect behavior change (COM-B)

Ways to create sustained behavior change to promote compliance to nutrition recommendations	
Target	**Example strategies**
Change capabilities Physical Psychological	· Assure the client is able to obtain food and follow specific feeding instructions · Employ the team to provide increased opportunity for questions/conversations after the visit · Provide education and credible resources · Create and maintain accessible information tailored to the needs of the individual client and pet
Change opportunities Environmental Social	· Check in soon after recommendation given to troubleshoot any problems · Follow-up appointments in person or via telehealth · Create environment at home to fit into routine and human-animal bond · Consider social incentives (enlist family, friends, other pet owner support)
Change motivations Belief in change	· Help the client identify and build new habits and routines · Acknowledge improved pet health · Celebrate success

care for veterinary patients. Michie et al[9] developed the COM-B model (**Table 1**), which may help identify three conditions that influence client behavior and compliance. Capability (C) and opportunity (O) influence motivation (M), and all three factors can influence behavior (B).[10]

Improving any of these three conditions could help the client change their behavior and thus compliance.

- **Capability** includes either physical and psychological ease or ability of the client to perform the behavior, including having the necessary knowledge and skills. Example: Is the behavior easy or difficult from a physical and psychological perspective?
- **Opportunity** includes the social factors as well as the environment around the client and patient, which either promotes or impedes a behavior. Example: How does the home environment (multiple pets, ability to roam) or the social aspects (support or opposition by family and friends) affect the behavior?
- **Motivation** is the drive, energy, or intent to perform a behavior, including habits, emotions, and thoughts. Example: To what extent does the person believe in the change?

These factors may not all be present to the same degree and targeting the barriers may help the client make the recommended changes. For example, upon hearing the diagnosis of their cat's chronic kidney disease, a client may be extremely motivated to "do everything possible" to minimize risk of progressive changes. However, when hearing the recommendation for a therapeutic diet change, both capability and opportunity may be limited in a multi-cat household where cats are group fed. The feeding environment may make it challenging to prevent the cats from eating one another's food. It can be psychologically challenging if owners perceive a new food is not as palatable to their pet. Evaluating and troubleshooting challenges can lead to strategies for improved patient care, because a combination of motivation, opportunity, and capability are important to promote client compliance. This may be an iterative process, in discussion with the pet owner, involving them in decisions about what changes they are able and willing to do at the time of the recommendation. By involving the pet owner and learning about their perspectives, willingness, and abilities, a tailored client-patient-specific treatment plan can be mutually developed and agreed upon. This concordance may not be the "gold-standard" treatment but could be a compromise in some aspects of the food choice or feeding plan. However, ultimately, this could achieve improved and sustained patient care because the client has participated and agreed on the plan. Studies have shown benefit from tailoring treatment to the patient and client and supporting the client's decision-making.[11]

Another model of behavioral change can provide practical strategies for communicating with clients to help determine if or when a client is ready to share

in developing therapeutic interventions. By using Prochaska's[12] transtheoretical model (stages of change, SOC) to identify a client's "readiness" for change, the VHCT can better understand the change process, successfully partner with pet owners, and customize recommendations that best suit each client's needs—in other words, to use the "right" approach for the "right" client at the "right" time.[13,14] Approaching clients when they are ready to act on advice will improve success and use time and resources more efficiently. In many instances, engaging an owner in a potentially emotional conversation regarding nutrition when they are not open to change may instead reinforce their previously held beliefs or resistance to nutritional recommendations. Pursue methods of communication and the timing of recommendations based on client receptiveness. It may take time and several visits to establish rapport and build the trust necessary to move clients to the next stage. Visits may require a team approach, patience, and understanding, but the patient's health needs are better served and clients more satisfied when they partner with the VHCT in the nutritional care plan for their pet.

The stages of change are described and paired with communication strategies below.

1. **Precontemplation**. These clients are unaware or don't see a reason to change and referred to as naïve, unmotivated, or resistant. Clearly, they are not ready or willing to change.

   Communication tips: In reality, heavily investing in nutrition discussions that require significant change are unlikely to be effective for these individuals. This client is not motivated to change, yet it is equally important not to ignore the potential for malnutrition until the next annual examination. Express concern about the pet's health and recommend a near-term follow-up to monitor for any adverse effects. By conveying care and concern for the patient rather than judgment, the veterinarian can monitor both the patient and the client and be ready for further discussion or action when the client is more receptive.

2. **Contemplation.** The client acknowledges the problem and is considering the pros and cons of changing a habit or lifestyle action but has not yet committed to making the changes. These clients may be stuck "thinking about it," intending to change "soon."

   Communication tips: If "stuck in this stage," the client may need to learn more about the issues involved. Providing information and resources such as handouts or links to reliable web sites may give them necessary information and reinforce the message that their pet's health is a priority and malnutrition is a real health concern.

3. **Preparation.** The client is committed to change and plans to take action in the next month or sooner. The client has recognized a concern about appropriate nutrition for their pet and may have attempted some change (e.g., sought advice from online sources, a pet store employee, or trainer).

   Communication tips: Recruit these clients for action-oriented programs. Ask what they need to be ready to begin and how the VHCT can help them. A very useful question is: "What are you most concerned about?" This gives the client an opportunity to express perceived challenges which can be addressed upfront.

COMMUNICATION TIP

"By understanding models of change and using intentional and empathetic communication skills, the VHCT can establish trust, educate the client, and identify their readiness to change."

4. **Action**. The client has taken steps toward change with varying success. For example, the client may have selected a different pet food or changed feeding management. However, change is not considered a significant action unless it has eliminated risk of malnutrition or illness and provided complete and balanced nutrition.

   Communication tips: Acknowledge what was done if they made small changes, and ask what worked (or didn't) about those changes. This can identify barriers in capabilities, opportunity, or motivation (COM-B) which can be targeted for the action plan. Work with clients to design an individual plan that accounts for their pet's needs, their own schedule and lifestyle, helping them build healthy habits. For

example, when implementing a therapeutic diet, the diet should make up ≥ 95% of the pet's intake in order not to negate the benefit. Work with the client to find nutritionally acceptable treats and alternative activities in lieu of treats. Another example: There should be no additional treats, foods, or foods used to administer medications during a food elimination trial. Not only should the specific instructions be clearly outlined but plans to administer medications and preserve feeding routines should be made proactively with the client to set them up for success. Provide feedback and compliments on the patient's progress to encourage the client to stay with the plan. Make a plan for checking in and following up.

5. **Maintenance.** The client is actively working to sustain changes developed in the action plan.

   Communication tips: Celebrate the successes and ask about perceived challenges. Talk with them about potential challenges (e.g., other individuals in the household that do not feel the same way, or upcoming travel, holidays, or guests that can disrupt a feeding plan). Refine the plan as necessary based on client feedback so that they anticipate problems in the future and proactively strategize some possible solutions. Keep instructions specific and clear, tailored to the individual pet and client's abilities. Make a specific plan to support and follow-up.

SUMMARY

Excellent communication skills foster a collaborative partnership with pet owners which improves veterinary team efficiency and satisfaction, client compliance, and patient outcome. Communication is an essential tool for performing the nutritional assessment, not only in gathering important diet history information but in helping assess the pet owner's ability and motivation to follow the nutritional recommendations. By understanding models of change and using intentional and empathetic communication skills, the VHCT can establish trust, educate the client, and identify their readiness to change, as well as potential pitfalls and opportunities to develop new habits when feeding their pet. Ultimately, the goal of the veterinary health care team is to help the client understand their pet's health concerns and nutritional treatment options so that they can work together to agree on the best option that is achievable for that family and pet.

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TAKING A TEAM APPROACH TO NUTRITION

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KEY TAKEAWAYS

- All veterinary health care team (VHCT) members have a role to play in increasing utilization of nutrition in a veterinary hospital.
- The majority of the nutrition portion of a veterinary consultation is within the veterinary team's scope of practice.
- Nutrition can be easily integrated into existing practice protocols.

OVERVIEW

Nutrition has been recognized globally as the fifth vital assessment,[1] alongside temperature, pulse, respiration, and pain. Nutrition provides the base fuel for all species, with the potential for malnutrition to cause catastrophic effects on the patient's overall function and quality of life. Nutrition should be the cornerstone of both health maintenance and disease treatment, utilized independently or synergistically with other modalities of care. Nutrition assessments and recommendations should be provided by the veterinary team as a component of every visit, even if compliance is incomplete. When nutrition is neglected by their veterinary teams, clients will resort to less-reputable sources of information without the benefit of professional guidance.[2,3] A survey by the American Animal Hospital Association found that clients both trust and value veterinary insight on their pet's food, yet they often perceive a lack of a strong nutrition recommendation from their veterinarian.[4]

Time is a limited resource in general practice, presenting a potential barrier to effective nutrition assessments and consultations. Within the confines of the scheduled appointment, the general practitioner must manage a thorough assessment of all body systems while formulating and implementing a plan to maintain or manage health. Add in the challenges of a normal day such as staffing shortages, seasonal pressures, unscheduled emergencies, and an overburdened schedule, and it is easy to understand why nutrition may be neglected or omitted by even the most dedicated practitioner.

A further challenge in practice are the staggering rates of burnout in veterinary medicine, affecting all members of the health care team. In a recent survey, Kogan et al.[5] found that over half of veterinary technicians were suffering from burnout. Affected team members may be unable to perform to their full potential, require a period of absence, resign from their position, or leave the profession entirely. This can lead to a shortage of veterinarians and team members, adding further strain to an already overburdened practice.

Incorporating nutrition assessments and recommendations into routine clinical care can actually help provide solutions to some of these issues,

COMMUNICATION TIP

By working together, the veterinary health care team can ensure that all patients receive the best opportunity to be fed nutrition that will fuel and optimize life.

as team members are more satisfied in their roles when they feel that their skills and knowledge are fully utilized.[5] Veterinary technicians report increased job satisfaction, lower rates of mental health strain, and overall improvement in workplace experience when they perceive their role as adding value to the practice while fully utilizing their skills and being provided with opportunities for professional development.[5–7] Further, increased revenue from an improved nutrition program can help to fund competitive wages and allow for the recruitment of additional team members. Food

sales offer an alternative income stream with relatively low overhead when compared with the costs of other therapeutic modalities. The time commitment to the team is minimal when compared with interventions such as surgery.

Veterinary health care teams (VHCTs) are highly skilled, knowledgeable professionals with training in a variety of species' biological and psychological needs. Through extensive training and practical experience, team members understand patients' needs in health and illness, including confounding factors like environment, genetics, or life stage. Along with the veterinarian, members of the VHCT understand the nuanced requirements of both the healthy and ill animal and are prepared to implement a new nutrition protocol. Many team members have at least a foundational knowledge of wellness nutrition while registered veterinary technicians (RVT, or team members with similar qualifications) have a more advanced knowledge base. Within a practice, the entire VHCT plays a role in supporting the needs of the client, patient, and business. Many aspects of the nutrition assessment and consultation are already in place in other aspects of care. Minor modification of roles and responsibilities would minimally tax the individual while allowing for the implementation of an optimal nutrition protocol across the team. Most importantly, even the busiest practice can ensure that the needs of all patients are met in every appointment.

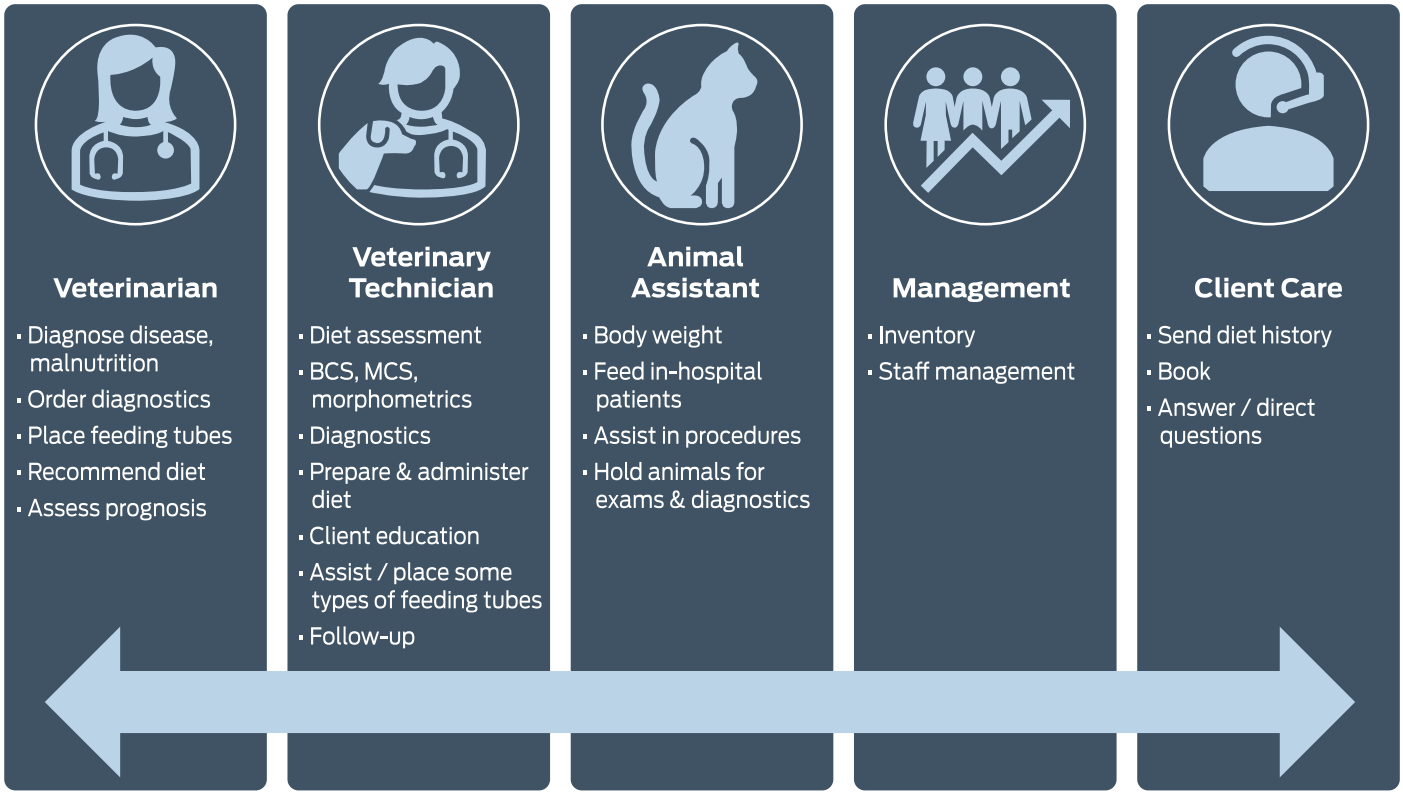
SCOPE OF PRACTICE (FIGURE 1)

The general practitioner may perceive that the entire nutrition consultation is their responsibility without allowing team members to assist within their abilities. A general review of the scope of practice can help recognize the potential expansion of nutrition services. As a focused guideline for nutrition implementation, this is not by any means an exhaustive list of all professional skills. Specific guidelines and laws may vary according to regulating bodies within countries, states, and provinces and should be verified. Individual comfort, knowledge, and skill will also play a role in maximizing the role of the team in nutrition. Additionally, the importance of professional development and continuing education for all team members should never be underestimated.

Veterinarian[8]

The veterinarian is the only team member who may diagnose; prescribe, order, or modify treatments or diagnostics; and perform surgery. As such, these duties

Figure 1. Scope of practice in a veterinary hospital



should be the priority for the veterinarian, and all other needs of the client and patient should be delegated to maximize team efficiency.

- Assessing patient through evaluation of history, physical exam findings, and diagnostics
- Ordering and interpreting of diagnostics
- Diagnosing and assessing prognosis
- Formulating of treatment plan
- Prescribing
  - Diet selection
  - Feeding plan
  - Surgical intervention
  - Medical management
- Reassessing patient to ensure successful management
- Performing surgery
  - Collecting biopsy samples
  - Placing feeding tubes
  - Surgical repair of digestive system

Veterinary Technician[9]

The RVT may also be recognized as an animal health technician or technologist (AHT), licensed veterinary technician (LVT), certified veterinary technician (CVT) or registered veterinary nurse (RVN). The term RVT will be used to encompass all licensed, credentialed veterinary technicians for the purpose of this chapter. They must meet the criteria set by their regulating body to achieve and maintain this title and may be self-regulated. Providing a wide array of technical skills, services, and assessments under the supervision or direction of a veterinarian, they assist veterinarians with complex procedures and the collection of diagnostic images and samples. They may also administer medications and nonsurgical treatments to patients. Their expertise in a broad expanse of veterinary topics also makes them prime candidates for client communication.

- Performing initial patient assessment, presenting findings to veterinarian for interpretation and discussion
  - Conducting nutrition assessment
  - Assessing body condition score (BCS)
  - Assessing muscle condition score (MCS)
  - Collecting morphometric measurements
  - Obtaining history
- Collecting, preparing, and processing samples for diagnostic assessment
- Obtaining diagnostic images
- Carrying out nonsurgical intervention under veterinary direction or supervision
  - Nasogastric or nasoesophageal feeding tube placement and general feeding tube management
  - Orogastric tube placement for emergency decompression or feeding
  - Gastric lavage
  - May include a new diet recommendation or modifications
  - Obesity management
- Performing veterinary calculations
  - Energy requirements
  - Feeding amounts
  - Ideal body weight
- Educating and communicating with clients
- Supporting diet transition
- Follow-up

Management

Clinic managers may also be veterinarians or veterinary technicians, or they strictly have managerial or business training and experience. Their scope of practice may vary, but examples of roles surrounding nutrition are described below.

- Inventory management
  - Sourcing of diets
  - Managing returns
  - Assessing inventory turnover
  - Managing supply interruptions and replacement items
  - Selecting which diets to stock and special order (with RVT/DVM)
  - Managing the web store for direct-to-client sales and automatic shipping
- Team management
  - Developing and implementing the nutrition program

Box 1. Veterinary Technician Specialist (VTS) in Nutrition

- Registered veterinary technicians with a passion for veterinary nutrition can further develop their careers by pursuing certification as a veterinary technician specialist in nutrition. These specialists will be required to pursue additional training in both practical skills and advanced knowledge beyond the expectations of a credentialed veterinary technician. They must demonstrate their expertise to the Academy of Veterinary Nutrition Technicians through an application process and exam. For more information, visit nutritiontechs.org.

  - Identifying and nurturing potential nutrition leaders
  - Providing professional development opportunities
  - Communicating with company representatives

Client Care

Client care professionals, office administrators, or receptionists may have formal academic training specific to veterinary care. They may also have received formal training for human medical practice or practically acquired training. Their skills in client communication are superb, and they may often fill the need for a veterinary assistant. Individual comfort level and scope of practice may vary based on their training and experience.

- Managing diet sales +/- inventory
- Reinforcing veterinary recommendation
- Addressing and directing additional client questions and communication
- Distributing and collecting diet history form via hard copy or digital
- Educating clients +/- RVT
- Follow-up +/- RVT

Animal Assistant

Animal care attendants or veterinary assistants may be formally academically trained or may have achieved their skills from practical, on-the-job training. If they have graduated from a National Association of Veterinary Technicians in America (NAVTA) program and successfully passed the exam, they may earn the title of approved veterinary assistant (AVA). They may also be veterinary technicians who are not licensed or students of a veterinary program. Their individual scope of practice and comfort level may vary.

- Weighing patients
- Feeding hospitalized patients +/- RVT
- Monitoring food consumption
- Fecal scoring

PUTTING IT INTO PRACTICE

When implementing a new or improved nutrition protocol, the best formula is to build from the success that the team has already established throughout all areas of practice. Rather than reconfigure individual responsibilities and roles, integrate nutrition into established responsibilities to better ensure a seamless implementation of the new program. Although all clinics are unique in their own needs and strengths, some basic principles can help to establish a successful program in a wide array of clinics, both large and small.

Existing within each practice is an established flow of client care touch points. First consider the existing distribution of established touch points within a practice. Each of these interactions can be highlighted as potential opportunities for the integration of nutrition, often with minimal additional time commitment.

Patient Care Touch Points

1) Booking and admission
2) History
3) Assessment
4) Treatment and discharge
5) Follow-up

Compare these touch points to the base structure of the nutrition consultation and consider where these steps could be integrated within existing protocols. Slight modification may be needed to fit the scope of practice of each team member.

Nutrition Consultation Steps

1) History
   a. Diet history
   b. Medical history

2) Assessment
   a. Patient: Identify nutrition risk factors
   b. Diet: Establish suitability of the current diet to the patient
3) Treatment: Modify or reinforce diet plan
   a. Discussion and formulation of plan with client
   b. Diet selection
   c. Feeding management: Amount, frequency, feeding method
   d. Communication of nutrition plan
      i. Diet features
      ii. Amount, duration, method
      iii. Transition
4) Follow-up
   a. In person
   b. Virtual
   c. Telephone
   d. Text

If each of the above steps are carried out by a single individual independent of other care needs, the nutrition consultation would certainly exceed practical time limitations. Instead, integrate the nutrition consultation within the team's existing patient touch points to maximize efficiency and minimize additional individual obligations.

AN EXAMPLE (FIGURE 2)

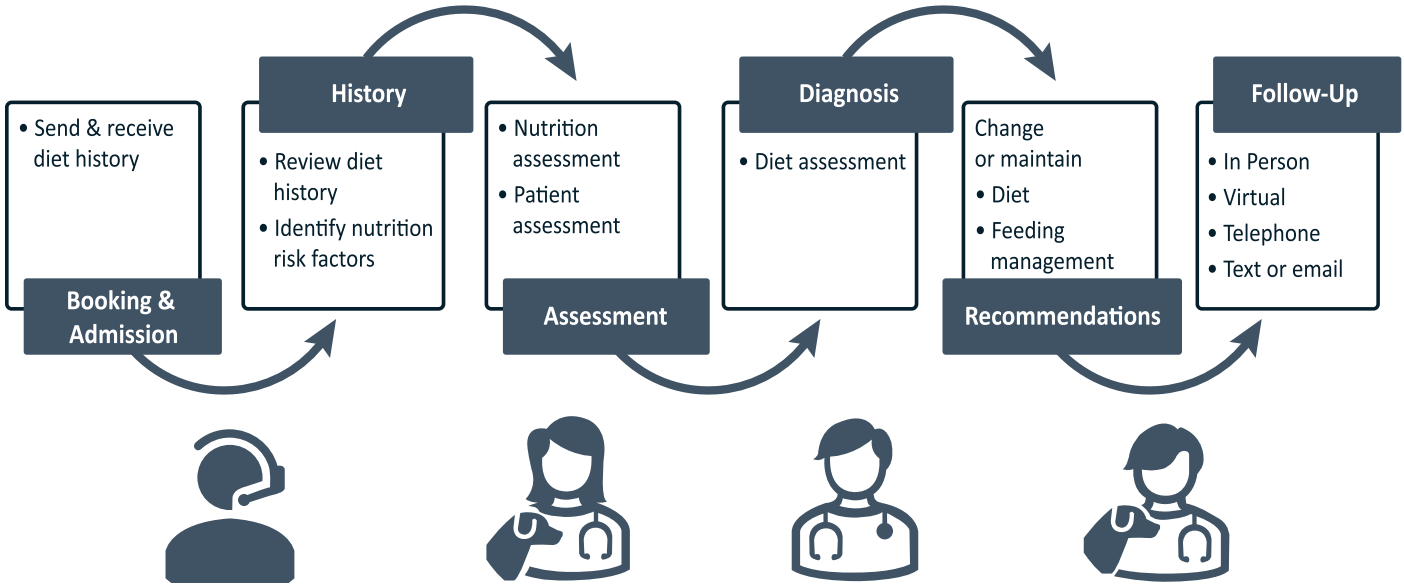
The client care team would distribute and collect the completed diet history prior to the consultation. When the patient arrives, they are admitted by the client care or animal care team who will obtain an updated body weight.

Prior to or during the appointment, the veterinary technician reviews the diet history form alongside the history and highlights risk factors such as changes in appetite or gastrointestinal function. The veterinary technician assesses and records BCS and MCS and performs relevant calculations.

The veterinarian can then integrate nutrition risk factors from the combined history into the overall patient assessment. If a new disease is diagnosed or suspected, a specific diet and feeding plan could be recommended with the treatment and diagnostic plan for the patient. If no diet change is indicated, this should be highlighted as well to encourage continued compliance.

Under the direction of the veterinarian, the veterinary technician can collect, prepare, or complete relevant diagnostics. If advanced nutrition intervention such as initiating feeding with feeding tubes is required, the RVT can assist or even place certain feeding tubes, calculate refeeding plans, and commence feeding. Nutrition management in the hospital can

Figure 2. Veterinary appointments tend to follow a general patient care protocol. Each of these touch points provides an opportunity to split the nutrition consultation into steps which can be seamlessly shared with the team.



Box 2. Establish a nutrition plan B

- A successful veterinary team is flexible! If a team is short staffed due to illness, vacation, or is occupied by an emergency, be prepared to shift responsibilities within appropriate scopes of practice.
- A separate appointment may be booked to address nutrition in exceptional situations, such as an unscheduled emergency interrupting the appointment. It also may be necessary to spend more focused time on nutrition, which may be to address misinformation or advanced nutrition plans. Consider booking these as a technician appointment via telehealth or in person to allow clients the additional time they need or consider including nutrition in a scheduled follow-up appointment. Some conditions, such as weight loss, may require a series of nutrition rechecks.
- Management tip: If the need to schedule these appointments is frequent, it may indicate a need for a nutrition block in the schedule, longer appointment times, or additional team members.

be implemented and managed by the RVT. They can educate clients on a change to the diet or feeding management, including gradual transition techniques, and address client concerns. The RVT can follow up with the client to answer additional questions, assess diet transition success, and review patient progress. This can be done along with other patient follow-up in collaboration with the veterinarian.

CONCLUSION

The ideal nutrition program will not overly tax any single individual on the team, but rather make sure that all members are able to contribute. By working together, the veterinary health care team can ensure that all patients in all appointments, on even the busiest day, receive the best opportunity to be fed nutrition that will fuel and optimize life.

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NUTRITIONAL MANAGEMENT OF PATIENTS WITH MULTIPLE CONDITIONS

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KEY TAKEAWAYS

- With at least one comorbidity, consider listing the desired nutritional management strategies for each disease to enable prioritization
- Many veterinary therapeutic diets can be successfully used to manage complex cases
- Consider a properly formulated homemade diet if needed or preferred by the client

NUTRITIONAL ASSESSMENT OF THE COMPLEX PATIENT

With advances in preventive health and in treatments for a myriad of diseases, the pet population is advancing in age. Most estimates indicate that the number of senior dogs and cats is increasing, and there is much interest in developing strategies for improving both quantity and quality of life.[1] Senior pets tend to develop various disease processes, and most but not all dogs and cats with complex comorbidities are older.

A comprehensive diet history is essential for guiding the development of a nutritional management plan for a complex patient. A complete nutritional assessment process considers the detailed diet history as well as other clinical data in order to correlate factors such as body weight trends, appetite, and calorie intake.[2] Serial subjective and objective data is invaluable for not only assessing prior response to specific dietary strategies, but also for evaluating and adjusting any implemented plan. Having a good understanding of patient status and the severity and impact of various comorbidities will enable prioritization of nutritional management strategies.[3,4]

In some cases, one or more concurrent diseases will be less or not at all responsive to specific nutritional strategies. Therefore, prioritizing dietary modifications will be more straightforward. In other cases, the major diseases will have aspects for which dietary modification can have a significant positive impact. If there is a need to consider two or more nutritionally responsive diseases, it is recommended to create a list of the targeted dietary strategies (**Table 1**). This will enable identification of any overlaps or conflicts, as well as help avoid overlooking any particular modifications that should be considered.

Common nutritionally responsive comorbidities:

- Pancreatitis plus chronic kidney disease
- Pancreatitis plus adverse food reactions
- Chronic kidney disease plus adverse food reactions
- Chronic kidney disease plus feline lower urinary tract disease
- Chronic kidney disease plus diabetes mellitus
- Chronic kidney disease and/or protein-losing nephropathy plus obesity

PRIORITIZING NUTRITIONAL MANAGEMENT STRATEGIES

Many strategies may overlap or be neutral for the implementation of dietary modifications. However, for some cases, compromises in strategies may be necessary. This may involve less aggressive modification, such as modestly but not severely reduced phosphorus concentrations. In other instances, a strategy may need to be prioritized lower or abandoned altogether. For example, a picky dog with a highly selective appetite and that is accustomed to a high degree of dietary variability may not accept a strictly limited and consistent food trial of novel ingredients. Similarly, instituting a strict and aggressive weight loss plan may not be feasible in an obese patient with significant comorbidities that require nutrient modifications.[5]

Table 1. Example dietary strategy prioritization lists for a complex canine patient with 3 comorbidities

	DIAGNOSIS		
	CKD stage 2, proteinuric, hypertensive	**Cardiac disease (MMVD Stage B1)**	**Obesity**
Strategies	Reduced protein, adequate amino acids	Adequate protein and amino acids (including taurine, arginine)	High protein
	Restricted phosphorus, controlled sodium and potassium	Controlled sodium and potassium	
	Supplemented select nutrients such as B vitamins, antioxidants, carnitine	Supplemented select nutrients such as B vitamins, antioxidants, carnitine	Fortified in nutrients including antioxidants and carnitine
	Supplemented omega-3 PUFA	Supplemented omega-3 PUFA	
	Energy-dense		Voluminous/high fiber, not energy-dense

In this case, most modifications overlap or are neutral to others, with the major exception being the protein concentration and energy density/volume. Strategies for cardiac disease do not limit implementation of those for either chronic kidney disease (CKD) or for obesity; however, CKD and obesity in the same patient presents some challenges.

Decisions regarding the management of this case would depend on the current degree and impact of obesity as well as the diet history and patient factors such as appetite quality. If significant calorie restriction is necessary to improve the body condition score, evaluation of the nutritional profile of the diet is necessary to ensure adequate nutrient intake. Consideration should also be given to modification of the weight loss plan, such as aiming for a slower rate of loss.

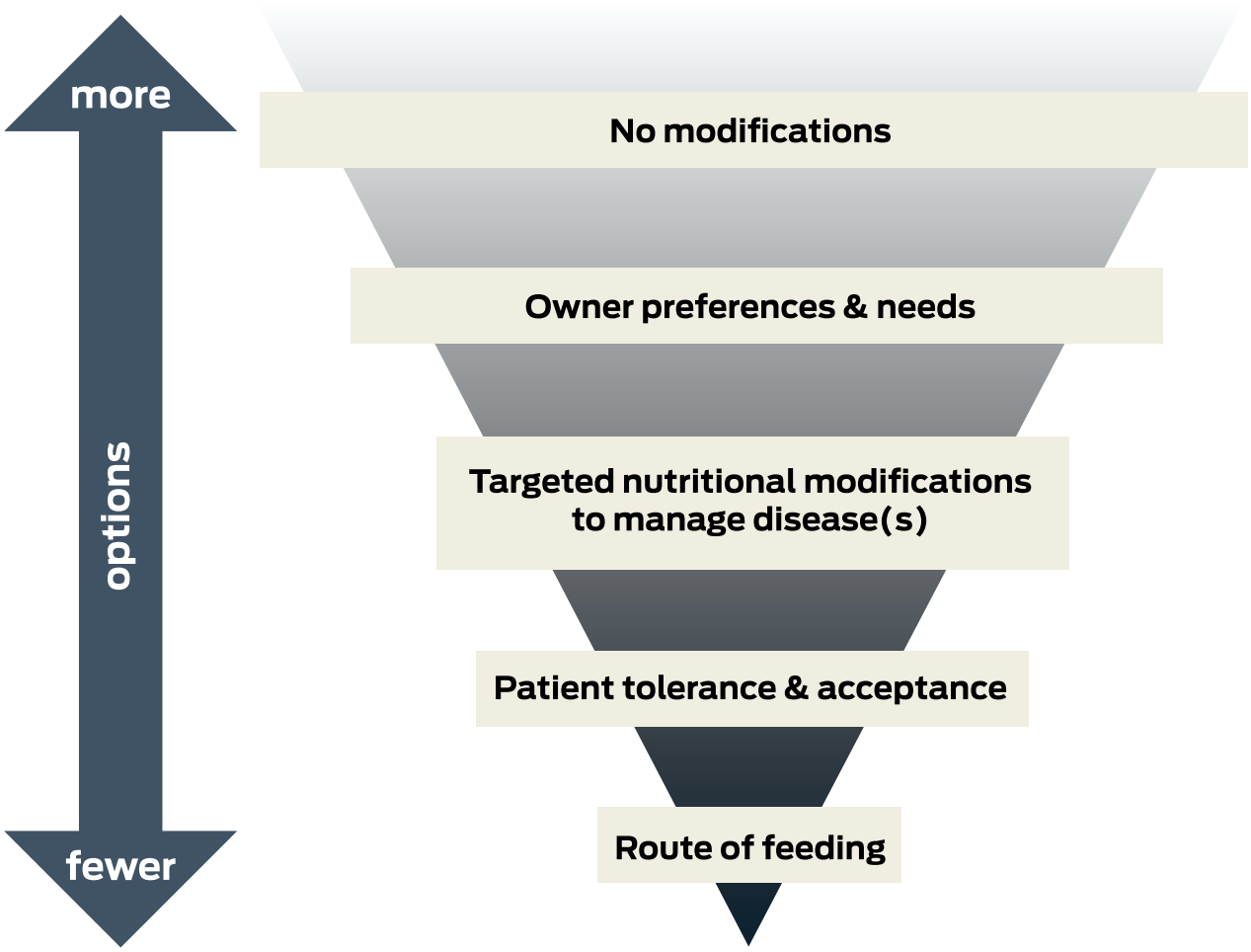
For overweight and obese animals, weight loss plans should only be instituted for patients that are otherwise stable and have good appetite. Close monitoring will help ensure that weight loss is intentional and at an appropriate rate.

Factors to consider when prioritizing nutritional management of disease processes:

- Impact on longevity (e.g., severity and chronicity of disease, patient age and status)
- Impact on daily quality of life (e.g., vomiting or diarrhea, pruritus, osteoarthritis)
- Impact on recurrence risk (e.g., urolithiasis, pancreatitis, cardiac disease)
- Expected timeline to see benefits of dietary modifications (e.g., fat restriction in lymphangiectasia vs. calorie restriction in obesity)

The patient's acceptance and tolerance of specific dietary components (ingredients, supplements, added water, etc.), forms (canned, kibble, etc.), and meal volumes may limit options as well. Additional criteria that meet the needs of the family and the patient will ultimately limit dietary choices (**Figure 1**). For example, a healthy cat that will eat anything, owned by a client willing to feed anything, has almost countless appropriate dietary options, while a hyporexic dog with chronic food-responsive enteropathy and chronic kidney disease plus a history of recurrent pancreatitis will have many fewer options. Finally, in some cases, the need to utilize a feeding tube and develop an enteral feeding plan will also limit diet choices.

Figure 1. With additional limitations on the nutritional management plan, fewer dietary options will be appropriate



DEVELOPING A NUTRITIONAL MANAGEMENT PLAN FOR A COMPLEX PATIENT

There are many dietary options in a variety of categories which may be suitable for an individual situation (**Table 2**). It is very useful to have access to product guides that provide nutritional information for veterinary therapeutic diets from several manufacturers. Well-pet diets may also be helpful for certain cases; up-to-date nutritional data for these can be obtained from the respective manufacturers. Having detailed nutritional profile information for a variety of products will enable comparisons of diets. Diets in any specific nutritional management category will be variable in nutritional profile as well as energy density and individual palatability, and selection of options at the extremes may be needed to address specific cases. It is very useful to know which options in specific therapeutic categories are appropriate for growth, which are lowest in fat or highest in fiber, and which may have other claims for disease management. For example, a clinician may aim to initiate a dietary elimination trial in a cat with suspected cutaneous adverse food reactions and a history of urinary stone disease. Review of the available veterinary therapeutic hydrolyzed diets can reveal the options that have a urolithiasis management claim. Similarly, dogs with a history of well-managed pancreatitis that develop chronic kidney disease should be fed a veterinary therapeutic diet formulated for renal disease and that has a fat concentration similar to the current diet. However, it should be noted that both therapeutic and well-pet diets are not uncommonly reformulated, while others are newly introduced or may be discontinued or backordered. Therefore, checking on the details and availability in order to provide current information is warranted.

For some cases, there will not be a suitable and appropriate veterinary therapeutic or well-pet diet, unless significant and potentially unacceptable

Table 2. Features of various categories of dietary options for management of veterinary patients

Commercial veterinary therapeutic diets		Commercial well-pet diets		Home-cooked diets	
Pros	**Cons**	**Pros**	**Cons**	**Pros**	**Cons**
More aggressive strategies possible (e.g., restriction of phosphorus or copper)	Cost (financial)	More accessible and affordable	Less aggressive strategies available	Ability to fully customize nutritional strategies	Cost (financial, time, space, effort)
Combinations of strategies to address various aspects of disease	Not as widely available; purchase must be approved by veterinarian	Wider range of options for flavors, diet forms (if appropriate for patient)	Nutritional profile information not as accessible	High palatability	Require input of qualified formulator (board-certified veterinary nutritionist)

Please note: Pros and cons listed are general considerations and do not apply to every situation or every patient's needs.

compromises in strategies are made. Similarly, there may be only one or two commercially available options, and if the patient does not accept or tolerate these, alternative plans should be considered. A balanced and customized home-cooked diet can be an excellent option for including a combination of strategies that are not available in commercially available products. These also tend to be palatable, and can be fully customized to meet the needs of the patient. Potential downsides of home-cooked diets include the increased effort and time as well as cost. In addition, even though many pets find homemade foods palatable, the nutritional profile may necessitate lower protein and/or fat, which may not be as readily accepted. Most pets find sources of protein and fat palatable, and are unwilling or unable to consume an often more voluminous, higher carbohydrate diet. In those cases, creative recipe solutions may be needed but can be very successful. For complex cases, an experienced board-certified veterinary nutritionist can be an invaluable asset to create a truly customized, nutritionally balanced and palatable diet, with additional troubleshooting support to allow for patient acceptance as well as client compliance and adherence.

Recommendations made to the owner should include the specific dietary product(s), amounts to feed in grams, guidance on feeding frequency, and specific instructions for any treats and foods for medication administration. Volumes are not accurate, and kitchen gram scales are relatively inexpensive and easy to use. Clients should understand the goals of the plan, in addition to which parameters will be monitored over time. It is also recommended to discuss a secondary plan in the event that the diet is not accepted or tolerated. At that point, the plan can be general (fiber modification, for example), or more definite (in terms of a specific diet or ingredient change). Setting expectations for reassessments and troubleshooting is an important part of successfully investing the family in the management plan.

MONITORING AND REASSESSMENT

In order to confidently evaluate the patient's response to dietary modification, follow up data and assessments are crucial. There are general monitoring parameters that apply to every case, such as body weight trends, appetite, gastrointestinal signs, and general well-being (attitude, activity level, engagement and family interactions). In addition, individual patients will have other parameters that should be monitored and that are dependent on the underlying comorbidities, such as serum concentrations of fasting triglycerides, vitamin B12, or phosphorus. Given that the status of many complex patients is dynamic, flexibility in the

COMMUNICATION TIP

Compromises in strategies may be necessary. This may involve less aggressive modification, or in some instances, a strategy may need to be prioritized lower or abandoned altogether.

prioritization of goals is warranted, and this process is typically repeated at each recheck. It is also important to confirm adherence to any recommended diet and supplements. Ensuring that the plan is working well for both the family and the patient will help promote better outcomes and guide any necessary troubleshooting.

CONCLUSION

The goals of developing a nutritional management plan for a complex case are to identify any diseases that are responsive to dietary modification, balance any conflicting strategies based on patient status and objective clinical data, and then implement appropriate and feasible changes. Finally, comprehensive reassessments are part of the iterative process, and this is necessary to refine the plan if warranted. Successfully managing a patient with comorbidities can be both a challenging and rewarding process. Parameters that define successful outcomes in individual patients may vary, and should be determined and revisited as needed.

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PRACTICAL TOOL: GUIDELINES ON SELECTING SUPPLEMENTS

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The National Academy of Sciences–National Research Council (NAS/NRC) defines a pet supplement as "any substance for oral consumption by horses, dogs, and cats, whether in/on feed or offered separately, intended for specific benefit to the animal by means other than provision of nutrients recognized as essential or for provision of essential nutrients for intended effect on the animal beyond normal nutritional needs, but not including legally defined drugs."[1]

In the United States, the Food and Drug Administration Center for Veterinary Medicine (FDA-CVM) regulates both food and drugs but does not currently maintain a separate category for "supplements" for animals.[2] In many other parts of the world, including Europe, supplements for dogs and cats are sold as complementary pet food. Regardless of the way supplements are regulated, it can be difficult to find specific guidance for veterinarians for use when considering use of specific supplements. However, the World Small Animal Veterinary Association Global Nutrition Committee maintains multiple resources that can aid practitioners in finding information about supplements for animals.[3] The United States Pharmacopeia (USP) Dietary Supplement Verification Program is also an excellent resource.[4]

While there are rigorously tested and efficacious supplements from reputable manufacturers, regulation for supplements is not as strict as for drugs or food. Having less oversight can lead to ingredients being fed to pets that are not needed, ineffective, contaminated, or products that fail to meet label claims. For example, in one study, most of the products purported to contain probiotics failed to meet the label claim.[5] In one recent meta-analysis, the data failed to find support for use of chondroitin-glucosamine, one of the most frequently recommended supplements for pets in many countries.[6]

Box 1 contains a 6-point practical checklist that owners or veterinarians should consider using before feeding a supplement. The veterinary health care team is the primary source of information, and each veterinarian should use the resources discussed and review the scientific literature prior to using a supplement in their patients.

Box 1. Supplement selection checklist

1. Is the manufacturer reputable?
2. Is there is a known need for each ingredient in the supplement?
3. Is the amount of ingredient being provided safe for the species (more may not be better!) and not already provided by the dog's or cat's complete and balanced diet?
4. Can the company selling the product provide some form of quality assurance?
5. If the supplement contains a probiotic, can the company provide data showing that the suggested minimally effective bacterial count is present at the end of the suggested shelf life of the product?
6. Can some level of evidence be provided showing that the supplement being considered has benefit to the species in question? The following are listed as highest to lowest evidence.
   a. Meta-analysis including at least the ingredient but preferably the specific product
   b. Peer-reviewed, published placebo-controlled trial
   c. Peer-reviewed, published open trial
   d. Company performed trial provided to consumers for scientific review
   e. Wide support by veterinarians on social media
   f. Company data on file, but not shared for scientific review

If the answer is NO to any of the checklist questions, that supplement should not be recommended or fed. If there are multiple supplements available in a category, preference should be given to the specific products that have been used in peer-reviewed clinical trials.

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GLOSSARY OF NUTRITION TERMINOLOGY

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A

AAA – see aromatic amino acid

AAFCO – see Association of American Feed Control Officials

Absorption – the passage of nutrients and/or substrates into and/or across tissues and cells

ACEi – see angiotensin converting enzyme (ACE) inhibitor

Acromegaly – see hypersomatotropism

Acute – the term used to describe a sign or disease having a rapid onset and, typically, a short duration (less than 2–3 weeks)

Acute diarrhea – one or more episodes of diarrhea lasting less than 3 weeks

Acute on chronic diarrhea – the presence of acute diarrheic episodes in an animal with ongoing gastrointestinal disease

Acute-phase protein – a protein whose serum concentration is directly affected by inflammation; positive acute phase proteins increase with inflammation, while negative acute phase proteins decrease with inflammation

Addison's disease – see hypoadrenocorticism

Adenosine triphosphate (ATP) – an energy-providing substrate that drives metabolic processes in living cells

Adherence – the degree to which an informed patient or owner will correctly follow the prescribed treatment or advice

Adsorbent or intestinal adsorbent – an antidiarrheal agent used to treat short-term diarrhea by binding offending toxins or pathogens for ultimate elimination via the gastrointestinal (GI) tract. Examples include smectite clay, kaolin-pectin, and bismuth subsalicylate.

Adverse food reaction (AFR) – any abnormal physiologic response associated with ingestion of a food and/or ingredient; may be immunologic or nonimmunologic

Aldosterone – a mineralocorticoid released from the adrenal gland that helps to regulate electrolyte and water balance

Alopecia – the abnormal loss of hair (partial or complete) from where it is normally present

Alpha-casozepine – a trypsin hydrolysate of alpha S1-casein, a protein found in cows' milk, that binds to GABA-A receptors in the brain. Considered a functional ingredient, often used to help reduce stress levels in dogs and cats.

Alpha-linolenic acid – an essential omega-3 polyunsaturated fatty acid with 18 carbons and 3 double bonds

(DL)-alpha-lipoic acid – a cofactor for mitochondrial respiratory chain reactions. Supplementation may improve mitochondrial function but can be toxic if too much is ingested, and cats are more susceptible to toxicity.

Amino acid – an organic (carbon-containing) compound containing an amino and carboxyl group, and the building block for all proteins

(5-) Aminolevulinic acid (5-ALA) – a natural δ-amino acid; hypothesized to improve lipid and glucose metabolism in obese animals

Ammonia (NH_3) – a product of protein metabolism and the precursor of urea; exists as a colorless alkaline gas

Ammoniagenic – ammonia-forming

Angiotensin – a family of hormones that act as vasopressors; angiotensin I (formed via renin acting on angiotensinogen) is the inactive precursor to the powerful vasopressor, angiotensin II

Angiotensin converting enzyme inhibitor (ACEi) – a substance that blocks the conversion of angiotensin I to angiotensin II, resulting in reduced blood volume and vasodilation ultimately causing lower blood pressure and reduced oxygen demand. Also used to treat glomerular proteinuria. Examples include benazepril and enalapril.

Angiotensin II receptor blocker (ARB) – a substance that blocks the angiotensin II receptor expressed in tissues including smooth muscles, resulting in reduced blood pressure. Also used to treat glomerular proteinuria. Examples include telmisartan and losartan.

Anorexia – the abnormal and complete loss of appetite

Antacid – any substance that neutralizes acids; typically administered to protect gastric mucosa against gastric acid

Antiemetic – a medication that treats nausea and vomiting via blockade of emesis-inducing receptors in the brain (i.e., vomit center). Examples include maropitant and ondansetron.

Antioxidant – a substance that either prevents formation of, or eliminates, oxygen free radicals. Examples include vitamin E, vitamin C, selenium, alpha-lipoic acid, carotenoids, and flavonoids.

Anxiety – a generalized emotional and physiological response in anticipation of a potential threat

Appetite stimulant – a medication used to encourage the voluntary intake of food. Examples include capromorelin oral solution, mirtazapine oral tablets or transdermal, and cyproheptadine.

ARB – see angiotensin II receptor blocker

Arginine – an essential amino acid that is key to the appropriate function of the urea cycle in hepatocytes

Aromatic amino acid (AAA) – an amino acid containing an aromatic (e.g., benzene) ring. Examples include tryptophan, phenylalanine, and tyrosine.

Arthritis – see osteoarthritis

Ascites – the abnormal accumulation of fluid in the abdominal cavity; if severe, may lead to abdominal distention

Aspiration – the inhalation of foreign materials, other than air, into the respiratory system

Assisted feeding – the provision of nutritional support when a patient is unable, or unwilling, to consume appropriate calories and essential nutrients. Methods include utilization of, or bypassing, the gastrointestinal tract (see enteral; see parenteral).

Association of American Feed Control Officials (AAFCO) – a United States non-governmental organization that develops pet food regulatory guidelines and standards that may be adopted by the State Departments of Agriculture. AAFCO guidelines may also be used in countries besides the United States.

(canine) Atopic dermatitis (cAD) – a genetically determined inflammatory and pruritic skin disease with a type 1 hypersensitivity response against environmental allergens

ATP – see adenosine triphosphate

Azotemia – the abnormal elevation of creatinine, blood urea nitrogen, and other nitrogenous metabolites in the blood; can be classified as pre-renal, renal, or post-renal

B

(vitamin) B3 – see niacin

(vitamin) B12 – see cobalamin

Balanced (diet) – a diet containing all essential nutrients in the appropriate concentrations and proportions for the individual being fed

BBB – see blood-brain barrier

BCAA – see branched-chain amino acid

BCS – see body condition score

Behavioral disorder – an expansive label including disorders of fear, anxiety, stress, conflict, panic (FASCP), impulsivity, phobia, and undesirable behaviors

Beta blocker – a medication that prevents adrenergic beta-receptor stimulation, thereby reducing heart rate and abnormal cardiac activity; classified as class 2 anti-arrhythmic drugs. Examples include atenolol, carvedilol, and propranolol.

Beta oxidation – the catabolism of fatty acids within the mitochondria, resulting in the production of energy

Bile acid sequestrant – a medication used to bind bile acids in the GI tract, making them unavailable for resorption, ultimately resulting in fecal excretion. Examples include cholestyramine, colestipol, and colesevelam.

Bioavailability – the degree to which a nutrient (or other substance) is available to the target tissue/cells after consumption

Birch sugar – an alternate name for xylitol (see xylitol)

Blood–brain barrier (BBB) – a semipermeable and selective layer of cells acting as a barrier between circulating blood and the extracellular fluid of the central nervous system

Body condition score (BCS) – an assessment of a pet's body composition, primarily body fat, using a combination of visual and tactile skills

Branched–chain amino acid (BCAA) – an amino acid with an alkyl side chain and methyl group branch. Examples include leucine, isoleucine, and valine.

Butyrate – one of the short-chain fatty acids (SCFAs) produced via fermentation of dietary fibers; the major fuel source for colonocytes

C

Cachexia – a multifactorial process characterized by loss of fat and muscle tissue that is associated with disease. It involves increased inflammatory cytokines, oxidative damage, inadequate delivery of nutrients, and impaired clearance of metabolic waste products, resulting in increased energy requirements and, often, increased protein degradation (lean tissue loss). Examples of causes include renal disease, cancer, and cardiac disease.

Calcium channel blocker – a class 4 anti-arrhythmic drug that blocks the passage of calcium through calcium channels in the heart and blood vessels, ultimately resulting in lower blood pressure and reduction of abnormal cardiac activity. Examples include amlodipine and diltiazem.

Calculogenic – any mineral that forms calculus (dental or urinary)

Calculus – an aggregation of minerals formed within the body, such as that formed in the oral cavity (tartar), kidney, or urinary bladder

Calorie density – see energy density

Canine IBD activity index (CIBDAI) – a reliable scoring index for inflammatory activity in canine inflammatory bowel disease (IBD) patients

Capability – the physical and psychological ease or ability of the client to perform the behavior, including having the necessary knowledge and skills

Carbohydrate (CHO) – a derivative of a poly (multi) hydric alcohol (usually an aldehyde or ketone), containing carbon, hydrogen, and oxygen. Typically, hydrogen and oxygen atoms are in appropriate proportions to form water after combustion. Examples include starches, fibers, and sugars.

Catabolic/catabolism – the cellular metabolic process that degrades or breaks down complex nutrients and molecules into smaller units

Central nervous system (CNS) – the portion of the nervous system containing the brain and spinal cord

CDS – see cognitive dysfunction syndrome

(copper) Chelating agent – a medication that lowers blood and tissue copper levels via binding and forming a soluble compound that can be renally excreted. Examples include d-penicillamine and dimercaprol.

CHF – see congestive heart failure

Chitosan – a natural compound derived from the polysaccharide chitin, used to treat hyperlipidemia by binding to negatively charged lipids

CHO – see carbohydrate

Cholangiohepatitis – inflammation of the hepatic and biliary system

Cholangitis – inflammation of the biliary system; typically, the intrahepatic ducts are most affected

Cholestasis – slowed or stopped flow of bile

Cholesterol – a subclass of lipids (sterols) found in animal tissues, and essential for cell membrane structure

Choline – a nutrient found in most tissues with many functions including formation of phospholipids and transport of fats/lipids

Chronic – the term used to describe a sign or disease having a duration longer than 2–3 weeks

Chronic diarrhea – the presence of persistent or intermittent diarrhea for longer than 3 weeks

Chronic kidney disease (CKD) – abnormal and irreversible decrease in renal function present for longer than 3 months

Chylomicron – a lipoprotein particle containing mainly triglycerides, phospholipids, and cholesterol. Enterocytes synthesize chylomicrons from digested lipids and secrete them into lymphatic vessels for systemic distribution.

CIBDAI – see Canine IBD activity index

Citric acid cycle – a series of mitochondrial reactions to release energy after the oxidation of calorie-providing nutrients (also known as Krebs cycle, tricarboxylic acid cycle, or TCA cycle)

CKD – see chronic kidney disease

CNS – see central nervous system

Cobalamin – a water-soluble nutrient, essential for many metabolic processes (e.g., formation of DNA and red blood cells); also known as vitamin B12

Cognitive dysfunction syndrome (CDS) – a combination of behavioral changes associated with aging. Observed behaviors may include anxiety, spatial/temporal disorientations, alterations of family interactions, and changes to sleep–wake cycle.

Colectomy – the partial or complete surgical removal of the colon/large bowel

Comorbidity – the presence of two or more diseases/medical conditions simultaneously

Complete (diet) – a diet containing all essential nutrients for that species

Complex carbohydrate – a polysaccharide with complex, long chains of sugars strung together; more energy is required for digestion, and thus, release of glucose

Compliance – the process describing how well a patient or owner carries out their prescribed therapy or recommendations

Concordance – a process of informed communication between the client and their pet's health care team, leading to an agreed-upon treatment and ongoing assessment plan

Conditionally essential (amino acid) – a non-essential amino acid that becomes essential in certain circumstances, such as pregnancy or disease conditions

Congestive heart failure (CHF) – a form of heart failure characterized by fluid accumulation in the pulmonary and/or venous system; often associated with retention of water and sodium

Constipation – a reduced defecation frequency and/or difficulty in passing feces

Cricopharyngeal achalasia – abnormal motor function of the cricopharyngeal sphincter; results in failure of relaxation and subsequent prevention of food from entering the esophagus during swallowing

Cushing's disease – see hyperadrenocorticism

Cystitis – inflammation of the urinary bladder

D

DCM – see dilated cardiomyopathy

Deficiency – inadequate nutrient concentration/ingestion resulting in impaired physiologic and metabolic functions

Degenerative joint disease (DJD) – any disorder/disease associated with progressive deterioration of a joint, articular surface, or articular cartilage (see osteoarthritis)

Deglutition – the process of swallowing; a complex process that clears food and drink from the oral cavity and pharynx into the esophagus and stomach at an appropriate rate

DHA – see docosahexaenoic acid

DI – see dysbiosis index

Diabetes mellitus (DM) – the presence of persistent hyperglycemia, resulting from either insufficient insulin secretion from pancreatic beta cells and/or insufficient response of insulin

receptors (to insulin) to maintain blood glucose concentrations in the normal range. Often seen with clinical signs, especially polyuria, polydipsia, weight loss, and polyphagia.

Diarrhea – an abnormal alteration in stool consistency (characterized by increased water content), with increased frequency, volume, and/or weight of feces

Diet-sensitive disease – a disease in which dietary modification can be used to lessen/mitigate associated clinical signs

Digestibility – the proportion of nutrients released from food following both mechanical and enzymatic digestion. Digestibility is influenced by both exogenous/dietary and endogenous/host factors.

Dilated cardiomyopathy (DCM) – ventricular thinning and dilation (and thus cardiac enlargement) that results in impaired systolic function and can lead to congestive heart failure (with atrial as well as ventricular dilation), arrhythmias, or a combination of the two. May be genetic, and/or idiopathic, and/or secondary to a nutritional deficiency.

Diuretic – a medication that promotes increased production (and thus elimination) of urine. Examples include furosemide, torsemide, and spironolactone.

Dissolution – the process of dissolving urinary stones

DJD – see degenerative joint disease

DM – see diabetes mellitus

Docosahexaenoic acid (DHA) – an omega-3 polyunsaturated fatty acid with 22 carbons and 6 double bonds; typically used for its anti-inflammatory properties

Dysbiosis – a reduction in microbial diversity (i.e., reduction in the number of different species) and/or changes in bacterial abundances that lead to altered production of bacteria-derived metabolites

Dysbiosis Index (DI) – a commercially available, analytically validated, PCR-based assay to assess the canine and feline GI microbiome in individual patients

Dysphagia – abnormal swallowing of food, liquids, or both

Dysrexia – abnormal feeding behaviors and/or patterns

Dysuria – painful and/or difficult urination

E

EAA – essential amino acid; see essential nutrient

EFA – essential fatty acid; see essential nutrient

Eicosanoid – a cell signaling compound derived from polyunsaturated fat metabolism. Examples include prostaglandins, leukotrienes, thromboxanes, and lipoxins.

Eicosapentaenoic acid (EPA) – an omega–3 polyunsaturated fatty acid with 20 carbons and 5 double bonds; typically used for its anti-inflammatory properties

Emesis – see vomiting

Endocrinopathy – a disease or syndrome associated with abnormal function of any endocrine organ

Endogenous – originating from within the body

Energy density – energy (kcal or kJ) per unit weight of food

Enteral (nutrition) – providing nutritional support via the gastrointestinal tract. Examples of routes include per os (PO)/by mouth/voluntary, esophagostomy (i.e., E-tube), nasoenteric (either ending in the esophagus [NE-tube] or gastric lumen [NG-tube]), gastrostomy (G-tube), and jejunostomy (J-tube).

(chronic) Enteropathy – a term referring to any disease/pathology of the intestine, but often used to describe a group of idiopathic diseases resulting in persistent or intermittent chronic gastrointestinal signs; subclassified into food-responsive, antibiotic-responsive, or immunosuppressive-responsive, depending on the response to treatment

EPA – see eicosapentaenoic acid

EPI – see exocrine pancreatic insufficiency

Epigenetics – behavioral and environmental factors that cause changes in gene expression

Epilepsy – abnormal electrical activity in the brain leading to episodes of temporary loss of control of behavior and movement (seizures)

Epileptogenesis – a process causing or leading to epilepsy

Esophagitis – an acute or chronic inflammatory disorder of the esophageal mucosa that occasionally involves the underlying submucosa and muscularis

Essential nutrient (e.g., amino acids, fatty acids, etc.) (EAA, EFA) – those nutrients that the body cannot make, or make in ideal/appropriate concentrations, and thus must be provided in the diet

European Pet Food Industry Federation – see FEDIAF

Exocrine pancreatic insufficiency (EPI) – a condition caused by insufficient synthesis and secretion of digestive enzymes by the exocrine pancreas

Exogenous – originating from outside of the body

F

FASCP – see behavioral disorder

FASS – see feline atopic skin syndrome

Fatty Acid (FA) – a carboxylic acid defined by its carbon chain length and the degree of hydrogen saturation. Fewer hydrogens mean more double bonds in the carbon chain, resulting in either mono- (one double bond) or polyunsaturated fatty acids (PUFAs).

FDA – see Food and Drug Administration

Fear – an emotional and physiological response to an imminent perceived threat

Fecal (microbiota) transplant (FMT) – the transfer of stool from a healthy donor into the gut of a recipient via oral capsules, endoscopy, or enema; also known as transfaunation

Fédération Européenne de l'Industrie des Aliments pour Animaux Familiers – see FEDIAF

FEDIAF – the trade association representing Europe's pet food industry. FEDIAF has produced nutritional guidelines that members follow. Countries outside of Europe may also use FEDIAF guidelines.

Feeding tube – a form of enteral assisted feeding utilizing a tube/catheter to administer nutritional support (see enteral)

Feline atopic skin syndrome (FASS) – an inflammatory and pruritic skin syndrome of cats manifested by a spectrum of reaction patterns; may be associated with IgE antibodies (a type 1 hypersensitivity response) to environmental allergens

Feline idiopathic cystitis (FIC) – a diagnosis of exclusion, where there is irritation or inflammation of the urinary bladder that has no known cause

Feline lower urinary tract disorder/disease (FLUTD) – any disease affecting the lower urinary tract in felines; clinical signs typically manifest as dysuria, hematuria, pollakiuria, etc.

(Feline) lower urinary tract sign(s) (LUTS) – clinical signs associated with lower urinary tract disorders in cats; include dysuria, hematuria, pollakiuria, periuria, and urethral obstruction

Fermentable (fiber) – a complex carbohydrate that resists mammalian enzymatic digestion but is able to undergo microbial digestion or fermentation

Fiber – a complex carbohydrate that is resistant to mammalian digestion and intestinal absorption**;** can be classified as soluble or insoluble, viscous or non-viscous, and non-fermentable or fermentable

Fibrate (fibric acid derivative) – a compound that functions by suppressing fatty acid synthesis, stimulating fatty acid oxidation, activating lipoprotein lipase, and noncompetitively inhibiting the enzyme diacylglycerol acyl transferase 2 (the enzyme that catalyzes the conversion of diglycerides to triglycerides), therefore leading to an overall reduction in serum triglyceride concentration. Examples include gemfibrozil, fenofibrate, and bezafibrate.

FIC – see feline idiopathic cystitis

Flatulence – excessive production of gases in the gastrointestinal tract

FLUTD – see feline lower urinary tract disorder(s)/ disease(s)

FMT – see fecal (microbiota) transplant

(United States) Food and Drug Administration – the regulating body within the United States government responsible for regulation of foods, food additives, cosmetics, and drugs

Food elimination trial – the gold standard for the diagnosis of food allergies and/or dietary intolerances. Involves exclusively feeding a specific diet (dependent on patient and dietary history) for a period of time (typically 4–12 weeks for dermatologic disease and 2–4 weeks for gastrointestinal disease). Recommended to be followed by a challenge with reintroduction of potentially offending foods. Also called a diet trial or an elimination diet trial.

Functional dietary ingredient or **functional ingredient** – an ingredient added to a diet for a specific purpose, without being required to make a diet complete and balanced

G

GABA – gamma aminobutyric acid; the primary inhibitory neurotransmitter in the mammalian brain

GAGs – see glycosaminoglycans

Gastroenteritis – inflammation associated with the stomach and intestine

Gastroesophageal reflux (disease) (GER[D]) – a syndrome resulting in the retrograde movement of gastric contents into the esophagus, often leading to esophageal irritation

GER(D) – see gastroesophageal reflux (disease)

GI(T) – gastrointestinal (tract)

Glucagon – a hormone produced and secreted by the pancreatic alpha cells in response to low levels of blood glucose. Ultimately increases blood glucose via activation of glycogenolysis.

Glutamine – a conditionally essential amino acid and a preferred energy source for rapidly dividing cells such as enterocytes

Glutathione – a potent hepatic antioxidant

Gluten – a protein associated with certain grain cereals (barley, rye, wheat, etc.), which provides elasticity and form to dough; comprised of gliadin and glutenin

Glycogen – a multi-branched, storage form of glucose

Glycogenolysis – the metabolic process of breaking down glycogen stores

Glycolysis – the metabolic process of breaking down glucose for energy

Glycosaminoglycans (GAGs) – compounds containing both polysaccharides and amino groups; often associated with connective tissues

H

H2 blocker – a medication that blocks histamine from binding to certain cells in the stomach resulting in reduced acid production. Examples include famotidine and ranitidine.

HE – see hepatic encephalopathy

Hematuria – abnormal presence of red blood cells in the urine

Hepatic encephalopathy (HE) – abnormal behavioral and neurological changes caused by the accumulation of ammonia or other false neurotransmitters secondary to severe hepatic disease or portosystemic shunting of blood. Not all liver diseases cause hepatic encephalopathy.

Hepatic lipidosis – a syndrome associated with protein-calorie malnutrition resulting in excessive accumulation of lipid within hepatocytes leading to hepatic dysfunction

Hepatitis – inflammation of the liver

HCM – see hypertrophic cardiomyopathy

HOCM – see hypertrophic obstructive cardiomyopathy

HUU – see hyperuricosuria

Hyaluronic acid – a glycosaminoglycan synthesized by chondrocytes and synovial cells; a component of joint fluid and articular cartilage, providing the joint with lubrication and shock absorption

Hydrolyzed (protein) – protein source that has been broken down to small peptides or amino acids by hydrolysis; thought to evade a type 1 hypersensitivity immune response by preventing cross-linking of two IgE antibody receptors on a mast cell

Hyperadrenocorticism – an endocrine disease characterized by abnormal, sustained increased release of cortisol, with associated clinical signs, that can be associated with primary disease of the pituitary or the adrenal glands; also called Cushing's disease

Hypercholesterolemia – an increased concentration of cholesterol in the blood

Hyperlipidemia – an increased concentration of lipids (i.e., triglycerides, cholesterol, chylomicrons, or any combination thereof) in the blood; see hypertriglyceridemia; see hypercholesterolemia

Hypermetabolic – changes associated with elevated metabolism and increased energy requirements

Hypersalivation – excessive saliva production

Hypersomatotropism – excessive production of growth hormone; also called acromegaly

Hypertension – systolic pressures exceeding 160–180 mmHg

Hypertriglyceridemia – an increased concentration of triglycerides in the blood

Hypertrophic cardiomyopathy (HCM) – the most common heart disease of cats, characterized by left ventricular wall thickening (observed via echocardiography) and in many cases subsequent mitral valve regurgitation, left atrial dilation, and congestive heart failure

Hypertrophic obstructive cardiomyopathy (HOCM) – a form of hypertrophic cardiomyopathy (HCM) where, in addition to left ventricular wall thickening, the anterior leaflet of the mitral valve moves against the left ventricular outflow tract in systole, causing an obstruction to outflow dynamics

Hyperuricosuria (HUU) – an inherited simple autosomal recessive defect, characterized by elevated levels of uric acid in the urine

Hypoadrenocorticism – an endocrine disease where the adrenal glands fail to produce sufficient hormones (typically both glucocorticoids and mineralocorticoids); also called Addison's disease

Hypometabolic – changes associated with lowered metabolism and lowered energy requirements

Hyporexia – reduced voluntary food intake; typically defined as animals eating less than 80% of their resting energy requirement (RER; see resting energy requirement)

I

IBD – see inflammatory bowel disease

Icterus – a yellowing of the body (skin, sclera, mucous membranes, etc.) due to excessive bile pigment in the blood

IDDM – see insulin-dependent diabetes mellitus

Inflammatory bowel disease (IBD) – a group of diseases associated with gastrointestinal mucosal and/or submucosal inflammation without evidence of a specific cause (see also chronic enteropathy). The disease is thought to arise from a combination of factors including genetic, intestinal microbiota, dietary, environmental, and immune function dysregulation.

Ingredient – a component of food that provides nutrients

Insoluble fiber – an indigestible complex carbohydrate that can increase fecal bulk; examples include cellulose, lignin, and hemicellulose

Insulin – a hormone produced and released from pancreatic beta cells in response to increased blood glucose levels; promotes storage/utilization of glucose, electrolytes, and amino acids

Insulin-dependent diabetes mellitus (IDDM) – diabetes mellitus that requires exogenous insulin administration (i.e., insulin injections) to control the clinical disease

Insulin resistance (IR) – an impaired response to normal levels of endogenous or exogenously administered insulin, typically resulting in hyperglycemia

International Renal Interest Society (IRIS) – an association of nephrology-focused veterinarians with the goal to help veterinary practitioners diagnose, understand, and treat renal disease in companion animals

International Society of Feline Medicine (ISFM) – a veterinary society created to be a practitioner-oriented resource for feline medicine and surgery

IR – see insulin resistance

IRIS – see International Renal Interest Society

ISFM – see International Society of Feline Medicine

K

Ketone – an organic molecule produced from triglyceride (i.e., fat) metabolism; also called ketone body. Examples include beta-hydroxybutyrate, acetoacetate, and acetone.

Key nutrients (of concern) – nutrients and their targeted ranges; dependent on the disease(s)/ medical issue(s) in question

Krebs cycle – see citric acid cycle

L

Lactulose – a synthetic non-digestible disaccharide comprised of glucose and fructose; used as both a laxative and treatment for hepatic encephalopathy

Laxative – a medication that facilitates or stimulates the expulsion of feces from the bowel

L-carnitine – a non-essential amino acid-related compound that improves mitochondrial function and is required for mitochondrial lipid metabolism; acts as a water-soluble vitamin-like substance

LCFA – see long-chain fatty acid

LES – see lower esophageal sphincter

Lipemia – circulating fat or lipid in the blood

Lipolysis – the metabolic breakdown of endogenous fat stores

Long-chain fatty acid (LCFA) – a fatty acid comprised of 16 to 22 carbons (see fatty acid)

Lower esophageal sphincter (LES) – a high-pressure area where the stomach meets the esophagus, functioning to prevent reflux of gastric contents; not a true sphincter

LUTS – see feline lower urinary tract signs

Lymphangiectasia – the dilation of lymphatic vessels in the mucosa and/or submucosa of the intestine and one of many causes of protein-losing enteropathy (PLE)

M

Maintenance energy requirement (MER) – the actual amount of energy required by a pet for weight loss, gain, or maintenance, depending on body condition score and patient goals. MER depends on life stage, spay/neuter status, age, activity level, and other factors and includes energy required for obtaining, digesting and absorbing food and energy for activity. MER in kcal/day is calculated as RER x MER Factor; this equation is not exact but estimates the actual energy requirements of a dog or cat. MER is also called daily energy requirement or DER.

Malabsorption – impaired intestinal absorption of nutrients

Maldigestion – impaired digestion of food, due to exocrine pancreatic dysfunction and/or intestinal brush border enzyme deficiency

Malnutrition – an abnormal state of nutrition, including deficiencies and excesses

MCFA – see medium-chain fatty acid

MCS – see muscle condition score

MCT – see medium-chain triglyceride

ME – see megaesophagus

Medium-chain fatty acid (MCFA) – a fatty acid comprised of 8 to 12 carbons; has a higher ketogenic yield compared with a long-chain fatty acid (LCFA). Examples include caprylic acid (C8; also called octanoic acid), capric acid (C10; also called decanoic acid), and lauric acid (C12); see fatty acid.

Medium-chain triglyceride (MCT) – a triglyceride comprised of medium-chain fatty acids; see triglyceride; see medium-chain fatty acid

Megacolon – persistent severe colonic dilation characterized by impaired colonic muscle tone/ function and loss of colon structure and function

Megaesophagus (ME) – focal or diffuse esophageal dilation and concurrent esophageal dysmotility; the most common cause of regurgitation in dogs and cats

MER – see maintenance energy requirement

Metalloenzyme – an enzyme that uses certain metals as a cofactor

(gut/intestinal) Microbiome – the collective of all microorganisms within the gastrointestinal (GI) tract

Motivation – the drive, energy, or intent to perform a behavior, including habits, emotions, and thoughts

Multi-strain probiotic – a probiotic product containing multiple species/genera of organisms; see probiotic

Muscle condition score (MCS) – an assessment of a pet's body composition (specifically, lean muscle tissue) using a combination of visual and tactile skills

Myxomatous mitral valve disease (MMVD) – a common cause of cardiac disease in dogs characterized by nodular thickening and expansion of the mitral and tricuspid valves, resulting in valvular regurgitation and murmur

N

NAC – see N-acetylcysteine

N-acetylcysteine (NAC) – a synthetic precursor to glutathione, a potent hepatic antioxidant

National Research Council (NRC) – an organization that compiles and collects research pertaining to different topics. Functions as the working branch of the National Academy of Sciences.

NH_3 – see ammonia

Niacin/nicotinic acid – a form of vitamin B3; an essential nutrient included in the diet; supplementation often used to help manage hyperlipidemia

NIDDM – see non-insulin dependent diabetes mellitus

Nitrogen free extract – see soluble carbohydrates

Non-insulin dependent diabetes mellitus (NIDDM) – a form of diabetes mellitus amenable to management with diet and drugs without the need for exogenous insulin; often characterized by insulin resistance or dysfunctional beta cells

Novel protein – a protein to which the pet's immune system has not previously been exposed and therefore should generally not elicit an immunologic reaction

NRC – see National Research Council

Nutraceuticals – foodstuffs that provide both nutritional and medical benefits

Nutrient – a metabolically useful component of ingredients and food; can be classified as essential or non-essential

Nutrient density – nutrient-to-calorie ratio of a particular diet

Nutrient profile – the unique nutrient composition of a particular diet

Nutritional assessment – an evaluation that includes consideration of animal-specific factors, diet-specific factors, feeding management and environmental factors, and human factors; performed in addition to medical evaluation, it includes body weight, body condition score (BCS), muscle condition score (MCS), and a *complete* dietary history

O

OA – see osteoarthritis

Obesity – excess storage of body fat, resulting in increased body weight and body condition score (BCS)

Obstipation – severe constipation with an inability to pass feces

Odynophagia – painful swallowing

Omega/(n)-3 fatty acid – a fatty acid where the first double bond occurs between the 3rd and 4th carbon from the methyl terminal carbon. Examples include docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA).

Omega/(n)-6 fatty acid – a fatty acid where the first double bond occurs between the 6th and 7th carbon from the methyl terminal carbon. Examples include linoleic acid and arachidonic acid.

Opportunity – the social factors as well as the environment around the client and patient which either promote or impede a behavior

Osteoarthritis (OA) – a progressive degeneration of diarthrodial synovial joints which results in articular chondrocyte death, synovial inflammation, loss of normal joint fluid and cartilage, subchondral bone sclerosis, osteophyte

and enthesophyte formation, and ultimately loss of joint function and chronic maladaptive pain (see degenerative joint disease)

Oxygen free radical – oxygen molecules with uneven numbers of electrons, resulting in instability and the likelihood of reacting with other molecules

P

Palatability – the state of being acceptable to taste; regarding trials, the preference of food measured by standard testing methods

Palmitoylethanolamide (PEA) – a naturally occurring bioactive lipid and endocannabinoid-like molecule produced on demand by damage-exposed cells; has been documented to counteract inflammation, itch, and pain

Pancreatic enzyme replacement therapy (PERT) – the supplementation of pancreatic enzymes to pets in need of additional digestive support; the mainstay of management in pets with exocrine pancreatic insufficiency (EPI)

Pancreatitis – an inflammatory condition of the pancreas

Parenteral (nutrition) – providing nutritional support through bypassing the gastrointestinal tract, typically via peripheral or central venous catheters

Paroxysmal dyskinesia – a neurological condition characterized by sudden involuntary movements

PEA – see palmitoylethanolamide

Periuria – urinating in inappropriate locations (i.e., outside of the litter box)

PERT – see pancreatic enzyme replacement therapy

Pharmaceutical – a medicinal drug; medication

Pica – eating or desiring to eat unnatural foreign materials

Pimobendan – a phosphodiesterase inhibitor with positive inotropic and vasodilatory effects; used in the management of heart failure

PLE – see protein-losing enteropathy

PLN – see protein-losing nephropathy

Pollakiuria – abnormally frequent urination

Polyphagia – excessive eating

Polyphenol – one of a family of organic compounds characterized by multiple phenol units; often used as a functional ingredient for antioxidant properties

Polysaccharide – a carbohydrate containing multiple sugar molecules bonded together

Polyunsaturated fatty acid (PUFA) – a fatty acid carbon chain with multiple double bonds

Post-prandial – after eating

Postbiotic – a preparation of inanimate microorganisms and/or their components that confers a health benefit on the host

PPI – see proton pump inhibitor

Prebiotic (fiber) – a substrate that is selectively utilized by host microorganisms conferring a health benefit on the host; typically, indigestible carbohydrates that promote growth of beneficial microorganisms, and can be divided into soluble/non-soluble and fermentable/non-fermentable fibers

Pre-prandial – prior to eating

Probiotic – a preparation of live microorganisms that, when administered in adequate amounts, confers a health benefit on the host

(NT) proBNP – N-terminal pro B-type brain natriuretic peptide; a biomarker used to assess severity of mitral valve disease, which may help to identify patients at risk for developing congestive heart failure

Prokinetic – a drug that enhances/stimulates gastrointestinal motility. Examples include metoclopramide, cisapride, and erythromycin.

Protein-energy malnutrition – malnutrition resulting from severe energy and protein deficiency

Protein-losing enteropathy (PLE) – a disease of the GI tract characterized by abnormal loss of protein via the stool

Protein-losing nephropathy (PLN) – a disease of the kidneys characterized by abnormal loss of protein via the urine

Proteinuria – an abnormal presence of protein in the urine, considered clinically significant when urine protein creatinine ratio (UPC) is > 0.5 in dogs and > 0.4 in cats

Proteolysis – protein (muscle) breakdown

Proton pump inhibitor (PPI) – a medication that reduces stomach acid production. Examples include omeprazole and pantoprazole.

Pruritus – itching

PUFA – see polyunsaturated fatty acid

Purine – a component of DNA, found in many animal protein sources

R

RAAS – see renin-angiotensin-aldosterone system

Refeeding syndrome – a condition that typically occurs when a patient (particularly a cat) with prolonged starvation is fed more nutrients than their body can assimilate, often resulting in fluid and electrolyte shifts (specifically phosphorus, magnesium, and potassium), thiamine/B1 deficiency, and altered glucose/fat/protein metabolism (among other clinical signs)

Regurgitation – the retrograde expulsion of food from the pharynx or esophagus

Relative supersaturation (RSS) – a mathematical calculation/ratio that predicts the ability of crystals to form or dissolve in urine

Remission – temporary recovery from clinical signs and disease

Renin-angiotensin-aldosterone system (RAAS) – an integrated hormone system responsible for controlling sodium (and other electrolyte) excretion that maintains sodium and water balance in healthy animals

RER – see resting energy requirement

Resting energy requirement (RER) – the number of calories required for maintaining homeostasis while the animal rests quietly in a thermoneutral environment. RER is often calculated as 70 x $BWkg^{0.75}$ although other equations exist as well.

RSS – see relative supersaturation

S

S-adenosyl-L-methionine (SAMe) – a potent antioxidant, and precursor to glutathione, that improves cell membrane integrity and rebalances monoamine neurotransmitter levels

SAMe – see S-adenosyl-L-methionine

Sarcopenia – a complex syndrome characterized by the severe loss of lean body mass and strength that may be seen as a part of the aging process

Satiety – a state of feeling full/satiated

SCFA – see short-chain fatty acid

Short-chain fatty acid (SCFA) – a fatty acid containing 2 to 6 carbons (see fatty acid). Produced in the colonic lumen by bacteria from fermentable fibers. Examples include butyrate, propionate, and acetate.

Silybin – the biologically active component of silymarin (extract from milk thistle), acting as a potent hepatic antioxidant

Silymarin – an extract derived from milk thistle

Small intestinal bacterial overgrowth (SIBO) – see dysbiosis

Soluble carbohydrate – a sugar or starch that requires little energy to digest and assimilate; a simple carbohydrate

Soluble fiber – a fiber that draws in and absorbs luminal water. Examples include psyllium, guar gum, and gum arabic.

Statin – a medication that functions by lowering cholesterol (in humans, statins lower LDL-cholesterol) with less potent effects on triglyceride metabolism. Examples include simvastatin and atorvastatin.

Stranguria – an inability to urinate or passing only small amounts of urine despite repeated attempts; typically indicates a physical or functional urethral obstruction and is usually accompanied by pain and discomfort

Supplement – a substance for oral consumption, whether in or on feed or offered separately, intended for specific benefit to the animal by means other than provision of nutrients recognized as essential or for provision of essential nutrients for intended effect on the animal beyond normal

nutritional needs, but not including legally defined drugs

Synbiotic – a mixture comprising live microorganisms and substrate(s) selectively utilized by host microorganisms that confers a health benefit on the host

T

Taurine – a beta-sulfur-containing free amino acid that has important physiological roles in cardiac and skeletal muscle, retinal function, and the central nervous system; considered an essential nutrient in cats as they cannot synthesize it

TCA cycle – see citric acid cycle

(L)-theanine – an amino acid that acts as a glutamate receptor antagonist and increases GABA, resulting in inhibitory and relaxing effects; often used as a supplement for helping to reduce stress in both dogs and cats

Therapeutic diet – food/diet designed to address the physiological compromises and clinical signs caused by disease, but rarely to cure the underlying disease

TLI – see trypsin-like immunoreactivity

Triaditis – the syndrome of concurrent inflammation in the pancreas, intestine, and liver in cats

Tricarboxylic acid cycle (TCA) – see citric acid cycle

Triglyceride (also known as triacylglycerol) – an ester consisting of a glycerol backbone attached to three fatty acids

(cardiac) Troponin – a cardiac-specific protein that can be assayed in blood samples; elevated levels can indicate cardiac damage and dysfunction

Trypsin-like immunoreactivity (TLI) – an assay that measures trypsinogen, trypsin, and some trypsin bound to protease inhibitors; species-specific serum trypsin-like immunoreactivity assays are used to diagnose exocrine pancreatic insufficiency (EPI)

Tryptophan – an essential amino acid; functions include acting as precursor to serotonin and melatonin, as well as niacin (in dogs). Considered a functional ingredient, often used for helping to reduce stress in both dogs and cats by increasing serotonin levels.

Tyrosine – an essential amino acid; functions include serving as precursor of dopamine, norepinephrine, and epinephrine

U

United States Department of Agriculture (USDA) – the United States governmental agency primarily responsible for domestic food production inspections, inspection of imported foods, and animal disease prevention in the United States

Urea cycle – a series of reactions in hepatocytes that removes ammonia from circulation by producing blood urea nitrogen for ultimate urinary excretion

Urethral obstruction – a blockage of the urethra, which conveys urine out of the body from the urinary bladder

Urolithiasis – the macroscopic accumulation of crystalloid material (uroliths or "stones") in the urinary tract

USDA – see United States Department of Agriculture

V

Veterinary health care team (VHCT) – a team of highly skilled, knowledgeable professionals with training in a variety of species' biological and psychological needs; includes veterinarians, veterinary technicians or nurses, assistants, client care representatives, practice managers, and other professionals

VHCT – see veterinary health care team

Vomiting – the forcible projection of stomach contents through the mouth; also known as emesis

W

Well-pet diet – a diet that can be purchased at retailers without a veterinary recommendation, designed to support healthy pets based on their respective life stages

World Small Animal Veterinary Association (WSAVA) – a global federation representing more than eighty veterinary medical associations around the world, with goals to promote animal health

and welfare and advance quality and availability of medical and surgical care

WSAVA – see World Small Animal Veterinary Association

X

Xanthine oxidase inhibitor – a substance that inhibits the conversion of both hypoxanthine to xanthine *and* xanthine to uric acid. An example is allopurinol, which is used in the management of urate uroliths.

Xylitol – an artificial sweetener that is toxic to pets, leading to hypoglycemia and potential hepatic damage; also called birch sugar

Z

Zymogen – an inactive form of an enzyme that is activated by another enzyme; also known as a proenzyme

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