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Nutritional Support of Pets with Cancer

The Oncology Working Group of the World Small Animal Veterinary Association defines cancer as "the process of body cells or tissues dividing uncontrollably, invading local tissues and potentially then undergoing regional metastasis or distant metastasis" (WSAVA 2021). What causes these abnormal cells to develop is unknown, and probably multifactorial, but once established, they alter the homeostasis that once existed in the pet. These cancer-induced changes may result in local or systemic alterations in metabolism that are leveraged to benefit survival of the cancerous cells, resulting in progressive malnutrition of the host (Argiles 2005). It has been proposed that there are 4 phases of metabolic disturbances as cancer establishes and advances (Saker 2010):

1. First is the subclinical stage, or silent phase, where obvious signs are not apparent and alterations in blood may occur, such as hyperlactatemia, concentrations of amino acids and hyperinsulinemia.
2. In the second phase, there is decreased appetite, lethargy and mild weight loss, which indicates advancing malnutrition.
3. The third phase is characterized by the loss of body fat stores and protein from labile sources such as muscle. This progression of systemic changes with cancer is often manifested clinically as decreased appetite, vomiting, diarrhea, lethargy and weakness. Continued presence of these metabolic changes and accompanying malnutrition has the potential to impair response to medical treatment. Pet parents often equate decreased appetite as suffering and choose to have their pets euthanized at this time.
4. The final phase is recovery or remission associated with improved clinical status; however, metabolic alterations may linger.

Food Acceptance

The 2016 AAHA Oncology Guidelines for Dogs and Cats states, "The most important dietary consideration for canine and feline oncology patients is that the ration is palatable and eaten; otherwise, it has no benefit" (AAHA 2016). Although some decrease in food intake may be expected in older pets, when it is accompanied by unintended weight loss or other signs of disease, a veterinary evaluation is indicated. This should include a nutritional assessment so that a plan can be implemented to optimize food intake. The cause of anorexia in pets with cancer is multifactorial and therefore might require multimodal management to minimize its impact.

Nutritional Considerations

Food acceptance by pets is driven by the sensory properties of food such as aroma, texture and flavor. Pets may be initially attracted to food primarily based on its scent; however, in terms of food acceptance, texture plays as crucial a role as ingredients that influence taste. Most palatability research is proprietary to the manufacturer and therefore not publicly available; however, there is an extensive body of work evaluating factors that influence acceptance of foods by pets. Shape, texture, density, aroma, taste enhancers, processing techniques and other technical aspects of producing food can be used by manufacturers to develop highly palatable foods.

Energy Balance (Caloric Intake)

Cachexia, a complex metabolic syndrome associated with underlying illness, is characterized by a loss of muscle mass with or without a loss of fat (Saker 2021). In adult dogs and cats, the prominent clinical feature of cachexia is weight loss, which is associated with decreased quality of life and poor prognosis (Saker 2021). Studies have shown that weight loss and underweight statuses are present, and that affects survival in dogs and cats with cancer (Michel 2004, Baez 2007). Dogs with osteosarcoma or lymphoma who were underweight at time of diagnosis had a significantly shorter survival time when compared with normal or overweight dogs (Romano 2016). Evaluation of historical weight records from newly diagnosed dogs with cancer revealed that 37% of dogs had lost weight from their historical recorded value (Michel 2004). Evaluation of body condition score (BCS) at time of examination revealed that dogs with cancer had a lower prevalence of being overweight and suffering from obesity (Weeth 2007). Body condition score in cats with lymphoma revealed that 56% had a BCS of 5 on a 9-point scale (Baez 2007). Survival time of this cohort of cats was 3.3 months compared with the 16 months for those with a BCS > 5/9. The cause of weight loss may be multifaceted, ranging from inappetence, increased basal metabolic rate attributable to cancer burden, alterations in taste preference (form or flavor), negative effects of treatment modalities or alterations induced to host metabolism that impair utilization of key nutrients. An example of the latter is the well-described Warburg Effect, where some cancerous growths prefer glucose as a substrate but utilize it inefficiently via anaerobic metabolism. This results in a high consumption of glucose with a net release of lactic acid, which is then recycled by the liver and is a net energy loss to the host (Wakshlag 2019). Increased basal metabolic rate has been documented in dogs with osteosarcoma but not in other types of cancer (Wakshlag 2019). This suggests that weight loss is more attributable to anorexia or other processes, and it re-enforces the importance of palatability to assure adequate calorie intake.

Nutritional Considerations

It is vitally important to maintain a positive energy balance in patients with cancer. Without adequate caloric intake, dogs and cats will begin to utilize glycogen stores, adipose tissue and labile protein to compensate. The simplest way to increase the energy density of the food, and thus calories, is to add fat. It has been suggested that fat be 25-40% of the dry matter content of the food in pets with cancer (Saker 2010). An exception is pets with known fat sensitivities, such as pancreatitis, hyperlipidemia and chronic enteropathy with lymphangiectasia, who should be managed with lower-fat and highly digestible foods.

Protein and L-Carnitine

Loss of lean body mass is an indicator of amino acid and protein malnutrition, which is detrimental to host survival. Because cats and dogs do not have storage reserves of protein (in contrast to fat or carbohydrates), any physiological state that results in a negative nitrogen balance also results in a loss of normal functions performed by protein. Once a loss of muscle mass is observed, it is safe to assume that protein malnutrition exists. Other examples where protein malnutrition would be manifested include immune function, gastrointestinal (GI) function, cell signaling and other protein-dependent physiologic systems. Loss of lean mass usually is attributed to increased turnover of protein induced by cancer cells. However, other nutrients that help preserve muscle mass should also be assessed to assure they are not contributing to inefficient protein homeostasis. One such nutrient is carnitine, which has been shown to be deficient in advanced cases of cancer in people (Cruciani 2007).

Nutritional Considerations

Offering food with increased amounts of highly digestible protein is a logical choice for pets with cancer (Wakshlag 2019). This protein provides amino acids that may be utilized to help blunt nitrogen losses attributable to metabolism changes induced by cancer and its management. Recommended levels of protein in pets with cancer are 30-45% (dry matter) for dogs and 35-45% (dry matter) for cats, except for pets with kidney disease and some diseases of the liver (Saker 2014). In addition to the absolute amount of amino acids available in the food, the correct balance is also needed to promote efficient protein synthesis. There are a variety of methods to assess protein quality based on benchmarking the amount of amino acids present in the nutritional source to some standard. While providing appropriate levels and a balance of amino acids, other nutrients, such as l-carnitine, may help to spare lean muscle mass by promoting fat metabolism and reducing protein turnover (Varney 2020). A key point to remember is that providing appropriate amounts of high-quality protein and balanced amino acids to promote protein synthesis and maintenance of lean mass depends on maintaining a positive energy balance. Therefore, ensuring food acceptance and an adequate caloric intake are still the most important aspects of nutritional support for pets with cancer.

Carbohydrates

Recommendations for the ideal amount of digestible carbohydrates in pets with cancer are controversial, and there is tremendous variation with commercial pet foods containing 18% to > 50% carbohydrates (Kazimierska 2021). It has been suggested that foods for dogs and cats with cancer contain digestible carbohydrates on the lower end of this range (Saker 2014). However, this is based on data from dogs with specific cancers and treatment regimens, and the assumption that the Warburg Effect (where cancer cells consume glucose and produce lactate) is present, which is not true for all tumor types (Potter 2016). Furthermore, it has been difficult to prove that limiting dietary carbohydrates slows tumor growth even in those cancers that display the Warburg Effect. Recommending an optimal level of carbohydrates to limit tumor growth has therefore proved elusive. Alternatively, metabolic alterations induced by some cancers in the host include the appearance of insulin resistance and increased lactate (Ogilvie 2006, Wakshlag 2019). The combination of decreased insulin-mediated uptake of glucose into the host's cells and increased uptake by some cancer cells may lead to a negative energy balance in the host and preferential diversion of substrate to the cancer. In addition, hepatic recycling of lactate produced by cancer cells also results in a net loss of energy to the host (Wakshlag 2019).

Nutritional Considerations

Because of the metabolic alterations described above, it has been suggested that foods for pets with cancer should contain less than 25% digestible carbohydrates (Saker 2010, 2014). Evidence for this theoretical benefit is lacking scientific support and is derived from a specific cancer protocol that might not be appropriate for all cancer types (Freeman 2017). Because no ideal carbohydrate level has been established, and the potential for insulin resistance exists, it seems reasonable that a moderate level of carbohydrates (20-30% of dry matter for cats, 25-35% of dry matter for dogs) would be acceptable in a food supporting pets with cancer. By providing a moderate amount of calories from carbohydrates, the food will by default contain higher levels of fat and/or protein, which increases nutrient density. Thus, the increased fat to carbohydrate ratio may help shift the energy balance back in favor of the host, which could result in a more positive energy balance. Because pets with cancer may have difficulty digesting key nutrients (due to cancer or cancer treatments), providing foods with highly digestible macronutrients (including carbohydrates) may be helpful. Finally, it is advantageous to the production of dry foods to have a moderate carbohydrate level to allow for proper kibble formation and texture.

Omega-3 Fatty Acids

Long chain omega-3 fatty acids have been reported to have anti-cachectic effects in animal models (Cowing 2001, Saker 2006, Huhmann 2010). Eicosapentaenoic acid (EPA), an omega-3 fatty acid, has been shown to preserve lean muscle by interfering with the ubiquitin-dependent protein degradation pathway (Saker 2021). Omega-3 fatty acids such as EPA and docosahexaenoic acid (DHA) have also been shown to blunt the upregulation of inflammatory mediators that promote tissue wasting in cancer (Cowing 2001, Tanner 2008). Clinical studies in pets are very limited, and the few studies that do exist suggest a positive benefit to feeding long-chain fatty acids. However, excessively low omega-6 to omega-3 ratios have been associated with concerns about platelet reactivity and clotting times in cats as well as alterations in immune function in dogs (Saker 1998, Wander 1997).

Nutritional Considerations

It has been suggested that foods for dogs and cats with cancer should contain increased amounts of omega-3 fatty acids to help manage inflammation, which is involved in the pathogenesis of cancer. It is recommended that a reasonable portion of the omega-3 fatty acids are of the long-chain type (> 20 carbons), which is most easily obtained from fish oils. Evidence to substantiate an appropriate absolute amount and ratio of omega-6 to omega-3 fatty acids for general support of pets with cancer has yet to be fully determined, and the available recommendations for dogs with cancer are specific for a certain treatment methodology in specific types of cancer (Saker 2014.) However, fortification with moderate amounts of omega-3 fatty acids, from marine oils and other ingredients, at a moderate ratio of omega-6 to omega-3 (ranging from 3:1 to 5:1) is considered reasonable.

Prebiotics

One overlooked area of nutrition in pets with cancer is the GI microbiome. Many pets with cancer, with or without treatment, will develop adverse GI signs including diarrhea or constipation. These may result from the cancer, its treatment or the lack of appropriate nutrient support for the microbes in the lower GI tract. Cancer treatment in people has been shown to cause gut dysbiosis (Deleemans 2021). Similarly, dogs with lymphoma have been shown to have alterations in fecal microbiota as a result of cancer (Gavazza 2018).

Nutritional Considerations

The gut microbiome in dogs and cats is complex and impacts many disease states (Wernimont 2020). There are no consensus recommendations

for the amount or type of prebiotic fiber to provide to pets with cancer. However, recent discoveries have identified prebiotic compounds that are beneficial to pets and can help manage diarrhea in pets (Jackson 2019). For cancer, it seems reasonable that a mix of soluble (fermentable) and insoluble (non-fermentable) fibers in moderate levels may provide the necessary variety needed by the complex ecosystem within the GI tract to help promote a healthy microflora and optimize stool quality.

Evaluation of Cancer Patients

A nutritional assessment is used for early identification of malnutrition and cancer cachexia, and it should be performed as a baseline at the initial diagnosis of cancer and at each clinic visit to detect changes in the pet's condition and the need for adjustments in the nutritional plan. The whole process can be done very quickly, and much of the information can be collected by the veterinary technician or nurse prior to evaluation by the veterinarian. Engaging with pet parents about nutrition helps build relationships between them and the veterinary healthcare team. There are excellent online resources for the veterinary healthcare team that include descriptions of a nutritional assessment (Box 1), practical tips and checklists for having nutritional conversations with pet parents, and how to make a specific nutritional recommendation (AAHA 2021, WSAVA 2022).

Providing Nutritional Guidance for Pet Parents

People with pets who have cancer are usually engaged and motivated to do what's best for their pet. While they often consult many resources, including online, to learn and understand the options for their pet, they highly value advice and guidance from the veterinary healthcare team. In one survey of people whose pets had cancer, 96% said they trusted their veterinarian's advice regarding their pet's healthcare and 79% indicated the same trust regarding nutritional advice (Rajagopaul 2016). In the same survey, 100% believed nutrition played an important role in their pet's health and 85% said they would purchase a conventional pet food that met their pet's medical needs (Rajagopaul 2016).

Because of the interest of pet parents and the importance of proper nutrition for pets with cancer, the veterinary healthcare team is in an ideal position to proactively engage in a nutrition conversation with pet parents at the time of a cancer diagnosis. This is an opportunity to discuss/understand their goals (which almost always relate to quality and length of life), answer their questions, inform them about credible online sources of information and make a specific nutritional recommendation. Each nutrition support plan should be developed with specific goals in mind and tailored to meet the needs of each pet. General nutritional goals for pets with cancer include preserving lean muscle, minimizing metabolic and GI intolerance to food, and optimizing quality of life (Saker 2014). It is recommended to begin nutritional support at the time of a cancer diagnosis and continue past remission for at least 6 to 9 months or longer (Saker 2014). The reasoning is that residual alterations in nutrient metabolism associated with the presence of cancer cells persist for a varying period past treatment.

To increase the likelihood of food acceptance and long-term consumption, it is important to recommend a complete and balanced food with exceptional taste that meets the nutritional needs of each pet with cancer. Veterinary therapeutic foods have been recommended for pets with cancer instead of over-the-counter foods because therapeutic foods have more accessible nutrient information, the digestibility of key nutrients is likely higher, they may be appropriate for GI issues resulting from cancer treatment or concurrent diseases, and some contain specific nutrients or functional ingredients that may be beneficial, such as EPA, DHA and fiber (Raditic 2021). For pets who have waxing/waning appetites associated with cancer or its treatment, use of pharmacologic agents (e.g., anti-nausea), different food forms (wet, dry or a combination) and/or other management tools may help encourage food intake (Box 2).

Summary

Cancer is associated with metabolic alterations and can progress to cause clinical signs (decreased appetite, weight loss) that indicate malnutrition. Cancer treatments also may negatively impact appetite and cause GI signs. People with pets who have cancer are highly motivated to do what's best for their pet, and they highly value nutritional advice from the veterinary healthcare team (even as they also consult online resources). A nutritional assessment should be performed at the initial cancer diagnosis and repeated at each visit to determine the need to adjust the nutritional plan. Maintaining a positive energy balance via adequate food intake is critical in pets with cancer. This can be facilitated by offering a complete and balanced food with exceptional taste that meets the nutritional needs of pets with cancer (e.g., highly digestible protein with adequate amounts of essential amino acids, increased omega-3 fatty acids such as EPA & DHA, and a mix of soluble and insoluble fibers).

Box 1. **Key Components of a Nutritional Assessment (AAHA 2021)**

- Physical examination and diagnostic testing (as appropriate for the pet's life stage/disease)
- Complete food history, documenting everything the pet eats from the time it wakes up to the time it goes to bed, including any snacks or treats used in training
- Eating enthusiasm or changes in eating habits
- Daily/weekly exercise levels and activities
- Information on home environment factors:
  - How food is provided (meals or free feeding)
  - Form of food (dry, wet or a combination)
  - Possible confounding factors related to other pets or people in the home
- Current body weight, body condition score, muscle condition score and changes over time
- Calculation of a pet's specific maintenance energy requirement (bit.ly/3mgxZVe)

Box 2. **Tips for Encouraging Food/Caloric Intake**

- Reduce meal size and increase frequency of feedings during the day
- Adjust food texture to account for a pet's dental health
- Warm foods to enhance aroma and perceived taste
- Try appetite stimulants when anorexia is noted for more than 3 days
- Always consider assisted feedings when a pet is not consistently consuming a minimum of 66% of daily calories
- Attempt interactive feeding practices to increase interest in food, prompt activity and stimulate cognitive functions in older pets

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