

EAT THIS, NOT THAT? WHAT TO FEED THE PET WITH CANCER

Sue Ettinger, DVM, DACVIM (Oncology)

Dr Sue Cancer Vet PLLC

Sleepy Hollow, NY, United States

Following a diagnosis of cancer in their pet, owners often become concerned about diet, nutrition, and supplements. The owner may look to their veterinarian about what the “best diet” is to fight the cancer, to support the cancer patient, and/or adding supplements. Some owners may switch to home-prepared diets. In one study, 80% owners believed a diet change was necessary for their pet with cancer. Not surprisingly owners of dogs with cancer are more likely to feed their pets a non-conventional diet. It has been reported that 51% of owners with cancer dogs had a mistrust in their pet’s diet of conventional dry and canned foods.

Research on nutrition for veterinary cancer patients remains deficient and inadequate. However, the internet is full of convincing recommendations for diet and supplements. Many veterinary reviews focus on anorexia and cachexia, but there are sparse studies looking at feeding trials and nutrient profiles in pet cancer patients.

WHERE ARE OWNERS GETTING THEIR INFORMATION?

Owners are looking for 24-hour information support about the dog’s cancer, treatment options and diet. In a study by Bianco et al, a veterinarian was the most reported source of information when researching general pet health topics, pet nutrition and nutritional supplement. However, owners of dogs with cancer favor different sources of information and were more likely to consult social media groups and blogs than owners of healthy dogs for this information. They also spent more time researching these topics. In contrast, owners of healthy dogs are more likely to consult pet stores for this information.

COMMERCIAL VS HOMEMADE DIET

While commercial food was most likely to be fed to healthy dogs and dogs with cancer, owners of healthy dogs were 4.4 times more likely to feed dry commercial food. A recent study reported 61% of owners with dogs with cancer were feeding commercial food (dry or wet) as their primary diet type, and this is a 10% decrease from a previous study suggesting a decrease in conventional diet feeding. This coincides with an increase in homemade diets. In the Bianco study 39% of dogs with cancer were being fed a homemade cooked diet, and 18% a homemade raw diet. For dogs with cancer the odds of feeding a homemade cooked diet were 4.3 times the odds of healthy dogs, and 2.2 times more likely to feed a homemade raw diet.

This mistrust in conventional diets is associated with the worry that dry and canned diets contribute to cancer, the ingredients are of poor quality, a desire to avoid carbohydrates, and the belief that a home cooked or raw diet may provide superior nutrition. This distrust is impacting the decisions of pet owners on what to feed their dogs with cancer. An advantage of commercial diets prepared by a reputable manufacturer: These diets are tested in feeding trials and meet nutritional AAFCO standards. Therapeutic commercial diets, available with a veterinarian’s recommendation, undergo even more extensive testing and are intended for pets with various medical conditions.

Some owners choose to prepare a homemade diet (HMD) for the goal of feeding wholesome unprocessed foods. The suggested benefits/claims include increase vigor, improved hair coat, decreased allergies, less inflammation, less stool and odor, and weight control. Owners should be advised these diets need to be balanced to account to meet essential protein, fat, vitamin and mineral requirements, to avoid the development of significant deficiencies. Also consider consulting with a board certified veterinary nutritionist to assist in creating a complete and balanced homemade diet for your patients – especially important if the dog has medical conditions. Check out ACVN.org to find a nutritionist. Other helpful sites to help formulate a homemade diet include Balancelt.com and Petdiets.com

CANCER DIETS

Low-carb/No-carb Diets

Many online blogs say feeding carbs to our pets with cancer will feed the cancer cells and allow the cancer to flourish and worsen. In the 1920s Nobel laureate Otto Warburg discovered tumor cells show high rates of glucose uptake and lactate production even when oxygen is lacking - also known as anaerobic glycolysis. This led to the concept known as the Warburg effect and is based on this metabolic abnormality that a low- or no-carbohydrate diet can starve cancer cells. However, follow up studies on cancer cell metabolism have shown cancer cells can have metabolic flexibility which allows them to regulate carbohydrate, fat and protein metabolism up and down in response to microenvironment, nutrient availability and cancer treatments. Not all cancer cells survive with anaerobic metabolism only, and a low-carb recommendation for cancer patients is likely an oversimplification.

Carbohydrates are not universally bad and contain many valuable vitamins and minerals. Instead of generalizing all carbs are bad, I think we should be more critical of the carbohydrate source and quality. Despite fruits and vegetables being carbohydrates, they also provide naturally occurring phytochemicals, flavonoids, fiber, and vitamins. Such dietary agents are called chemoprevention because they have potentially cancer-fighting properties that promote cell death (apoptosis) in cancer cells – they help get rid of deranged cancer cells. Epidemiologic studies in people show protective effects of diets rich in fruits and vegetables. In humans, there are two major nutritional risk factors associated with increased cancer risk. They are diets low in fruits and vegetables and obesity.

Ketogenic Diets

A ketogenic diet is a high-fat, moderate-protein, and very-low-carbohydrate diet. The reduction of carbohydrates puts the body into a metabolic state called ketosis. During ketosis, the body starts breaking down stored fat, and hepatic ketogenesis produces ketone bodies to use for energy, in the absence of circulating blood sugar from food. For cancer patients, the rationale is to starve the cancer cells from glucose while normal cells use ketone bodies for energy. Traditionally, the ketogenic diet was only used in clinical settings to reduce seizures in children with epilepsy, but now there is interest in the diet's effectiveness in helping with other conditions, including cancer, diabetes, obesity, and cardiovascular disease. There is a veterinary therapeutic diet for dogs with seizures that contains medium-chain triglycerides. There are currently no studies to support ketogenic diets for veterinary cancer patients.

The concern with these two diet approaches is the lack of research showing efficacy or that support these nutrient profiles. These diets have higher protein which is contraindicated in patients with renal disease and some hepatic disease. Higher fat diets are contraindicated in dogs with conditions including pancreatitis and hyperlipidemia and can cause vomiting, diarrhea, regurgitation and/or affect gastrointestinal motility. In addition, since fat has more than twice as many calories as protein or carbohydrates, these diets can be an issue for overweight dogs.

Grain-free Diets

Like a low-carb diet, grain-free diets restrict carbohydrate-rich grains based on the idea that wolves did not eat grains in the wild. However, recent genetic analysis has shown dogs can genetically digest more grains than wolves, and dogs are adapted to better use grains than wolves for nourishment. It is interesting to note that grain-free diets are not necessarily low carbohydrate diets. There are other carbohydrates besides grains in a number of "grain-free" dog foods, including potatoes, legumes, tapioca, vegetables, and fruits. When veterinary nutritionist Dr. Cailin Heinze and colleagues at Tufts analyzed dozens of diets said to be good for dogs with cancer, about one in three of those labeled as grain-free did not meet their defined criteria for low-carbohydrate regimens.

Raw food

A raw diet is often recommended as it is minimally processed. Diets containing raw meat are at greater risk of bacterial contamination compared to commercial cooked diets, including harmful bacteria such as *Listeria*, *E. Coli* or *Salmonella*. A concern is patients undergoing chemotherapy may be immunocompromised and at increased risk. As these pathogens can also be a significant health risk to consumers, they should handle these products carefully.

Intermittent fasting

Intermittent fasting is also gaining interest in people for weight loss and health benefits and for pets with cancer. Instead of focusing on what to eat, the focus is *when to eat* – eating only during a specific time. After hours without food intake, the body exhausts glucose stores and shifts to burning fat. The rationale for cancer patients is to help sensitize the tumor cells to a more stressful environment and dampen tumor-associated inflammation. Normal cells enter a “cleanup” phase during fasting, in which damaged cell organelles and abnormal proteins are cleared, known as autophagy. Dysfunctional autophagy or a lack of it is thought to contribute to many diseases including cancer. Nutritional restriction can modify autophagy and may enhance the efficacy of anticancer therapies while protecting normal cells from the damage from chemotherapeutics.

One prospective randomized study documented a decrease in delayed-type chemotherapy-induced vomiting associated with doxorubicin administration in lymphoma dogs who were fasted for 24 hours (18 hours before and 6 hours after chemotherapy) (10% vs 67%). Fasting affects the cell cycle and reduces gastrointestinal cellular proliferation rates through G₁ cycle blockade. This can preferentially protect normal cells through altered cell signaling including down-regulation of insulin-like growth factor 1 (IGF-1); cancer cells are not protected as doxorubicin is preferentially toxic in the S-phase. More studies are needed to evaluate effects on tumor control and chemotherapy sensitization.

Supplements. Vitamin and mineral supplementation are rarely necessary in dogs who are eating complete and balanced commercial diets or home-cooked diets balanced by a nutritionist. These diets contain all essential nutrients in appropriate amounts. Yet in the Bianco study, owners of dogs with cancer were more likely to feed nutritional supplements than the owners of healthy dogs, and they added significantly more supplements for cancer dogs. Overall, 279 supplements were reported (vs 226 in healthy dogs). The most common supplements included marine-derived omega-3 fatty acids (9%), mushroom supplements (8%), cannabidiol (CBD)/THC products (8%), glucosamine/chondroitin (6%), multi/mixed supplements supporting immune function (5%), turmeric/curcumin (5%), probiotics (5%), and plant-derived omega-3 fatty acids supplements (4%). Although clinical studies are limited, the only supplement with reported benefits in cancer patients are long-chain omega-3 fatty acids (fish oil). Efficacy is likely related to anti-inflammatory and anti-cachectic effects of EPA and DHA.

Nutritional supplements are not benign and careful consideration should accompany all supplement recommendations. Regulation of dietary supplements is lacking, especially in veterinary medicine, where safety studies and quality testing may be limited or nonexistent. Contamination with ingredients not listed on the label is reported and can pose a significant safety risk to pets.

WHAT SHOULD A CANCER PATIENT EAT?

Patients suffering from cancer are known to have significant alterations in metabolism of carbohydrate, proteins, and/or fat. As a result, it is important to provide our cancer patients with appropriate nutritional management to adjust for the changes in their metabolism. This will ultimately aid in improving their quality of life, possibly increasing the effectiveness of cancer treatment and survival times. Nutritional management should focus on soluble carbohydrates, fiber, protein and arginine, fat and omega-3 fatty acids, while at the same time providing adequate caloric intake to maintain good body condition.

It is recommended that soluble carbohydrates comprise less than 25% of food on a dry matter basis. Both soluble and insoluble fiber aids in maintaining intestinal health, especially in pets undergoing cancer treatment. Increasing fiber, particularly prebiotic fiber, has been shown to help maintain optimal stool quality. Proteins provided for cancer patients should be easily digestible and provide the appropriate balance of amino acids. Requirements may be higher than those of healthy pets due to increased protein turnover associated with inflammation. Arginine is an essential amino acid, one of the building blocks of proteins. The appropriate dietary levels of arginine for cancer patients is unknown but a positive correlation exists. It is suggested that it should be >2.5% on a dry matter basis. Some cancer cells have difficulty using fats as an energy source, while normal tissue can, and this has led to the belief that providing diets high in fat may benefit cancer patients. Omega-3 fatty acids, especially those found in certain types of fish and fish oil, are probably the most important to consider for pets with cancer. Several human studies have suggested that increased levels of omega-3 fatty acids may protect against certain types of cancer. While this has not been shown in dog/cat studies, it has been demonstrated in cell and

rodent studies. Finally, there are many views on the use of supplementing diets with high doses of antioxidants. While some believe high-dose dietary antioxidants may improve effectiveness of cancer therapy through enhanced immune function, it is also thought that these same antioxidants can aid in the survival of cancer cells by protecting against damage by chemotherapy or radiation therapy. Avoiding excessive, supplementary levels of antioxidants during cancer therapy is recommended.

EFFECTS OF BODY WEIGHT AND UNINTENTIONAL WEIGHT LOSS

A priority for cancer patients is to maintain body weight or gain. Unintentional weight loss can result in decreased body weight and/or muscle mass due to disease. This may or may not be accompanied by gastrointestinal signs. Mechanisms of weight loss can be categorized by one of more mechanisms: anorexia and decreased appetite, compromised ability to eat or retain food, inadequate caloric intake, maldigestive/malabsorptive conditions, inability to utilize nutrients, cachectic conditions, and nutrient loss. Further, weight loss during cancer treatment can indicate a poor response, a reflection of more severe disease, loss of lean mass, progressive disease, or suboptimal nutrition. It is also a common indicator of quality of life.

Dogs with lymphoma that were underweight at diagnosis had decreased survival times vs those at ideal weight or overweight. Body condition score (BCS) was not prognostic for the osteosarcoma dogs in the study, and progression-free interval did not differ among BCS categories for either cancer. For dogs with LSA or OSA, dogs that gained weight by $\geq 10\%$ had improved survival times compared to those that gained $< 10\%$, maintained or lost weight. While it may be that dogs that live longer may have more time to gain weight, weight loss and muscle loss can also influence survival.

Cats may show a more cachectic response that results in excessive lean body wasting. Changes in body condition in feline cancer patients has been shown to be prognostic for survival. In 57 cats with neoplasia, body condition score was assessed, and multiple sites were assessed for muscle and fat mass using four-point scoring systems. Feline cancer patients had a mean BCS of 4.4 \pm 2.1 kg (1=cachectic, 5=optimal, 9=obese). Fat mass was reduced in both sites assessed in 60% of the patients. Muscle mass was reduced at all three sites assessed in 91% of the patients. Feline cancer patients having a BCS < 5 had a median survival time (MST) of 3.3 months compared to that of 16.7 months for cats with a BCS of ≥ 5 .

Anorexia is common in cancer patients before diagnosis and/or during treatment. Anorexia is a major owner concern, a common reason for discontinuation of chemotherapy and can exacerbate chemotherapy side effects. To prevent weight loss in our cancer patients, we must focus not only on anorexia but hyporexia (reduced intake) and dysrexia, including being "picky." Our hyporexic patients will benefit from nutritional interventions early. Cases with weight loss will require dietary management to increase caloric intake by increasing palatability, caloric density and potentially using a feeding tube. Adjustments should be made for comorbidities and/or food allergies or intolerances. Food aversions may develop during cancer treatment, and it is helpful to have several diet options and/or textures. The owner or veterinarian may consult a nutritionist if needed. Feeding strategies may include adding meals to increase frequency/decrease volume per meal, handfeeding or changing feeding location, changing flavor/texture of the food, including palatants, and adding appetite stimulants (Capromorelin/ENTYCE[®], mirtazapine, and/or anti-nausea medications like Maropitant/Cerenia[®]). Other medications to consider include gastric acid reducers such as proton pump inhibitors.

It is also important to treat inappetence and weight loss while you work-up and diagnose the cause of inappetence and weight loss with pharmacologic management to address nausea and poor appetite.

OBESITY AND OVERWEIGHT DOGS

In humans, obesity appears to promote some cancers by increasing incidence, tumor aggressiveness, recurrence, and fatality but the research in veterinary oncology is lacking. There may also be a difference in the impact of overweight vs obesity.

In conclusion, there is no set nutritional requirements or recommendations for the cancer patients in veterinary medicine. There are a variety of cancers and a lack of well controlled studies. Yet owners of

dogs with cancer are looking to other sources including social media for information. There are diet differences in the dogs with cancer vs healthy dogs including increased likelihood of a homemade cooked diet or homemade raw diet and more likely to receive nutritional supplements. It's important that we as veterinary professionals partner with our clients to try to make the best recommendations for the patient. The most important factor is a feeding a complete and balanced diet to meet the patient's energy requirements to prevent fat and muscle loss and to address anorexia and hyporexia before, during and after treatment.

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