

## CACHEXIA: WHEN ALL YOUR PATIENTS CAN EAT IS THEMSELVES

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Cachexia is a multifactorial syndrome characterized by severe, chronic, and progressive weight loss and muscle wasting, oftentimes accompanied by anorexia.<sup>1</sup> Cachexia is a complex syndrome characterized by severe, chronic, undesired, and progressive weight loss and muscle wasting, with or without loss of fat mass.<sup>2</sup> This syndrome is associated with an underlying disease, anorexia, inflammation, insulin resistance, and increased lean muscle breakdown.<sup>3,4</sup> In addition, changes in carbohydrate, lipid, and protein metabolism are seen as a consequence of altered cytokine activity.<sup>2,4</sup>

Unlike weight loss seen with starvation or anorexia, cachexia is distinguished by a loss of adipose tissue with accompanying loss of lean body mass, primarily muscle. Non-muscle protein as found in the organs is preserved in cachexia but not in starvation. Significant loss of mineral content in the bones can also be seen contributing to the overall weakness found in many cachectic patients.<sup>1</sup> This discussion will look at cachexia and the role nutrition plays in managing cachexia.

### STARVATION VS. CACHEXIA

Weight loss associated with disease differs from that seen with simple starvation. In cachexia, there is an equal loss of muscle and fat characterized by increased catabolism of skeletal muscle. During starvation, fat is mobilized first sparing muscle proteins, resting energy expenditure is decreased and glucose metabolism is reduced. In contrast, cachectic patients have normal or elevated resting energy expenditures and glucose turnover. Adequate nutrition will halt and reverse the metabolic alterations that accompany simple starvation but will not completely reverse the metabolic disturbances associated with cachexia.

This loss of lean body mass has a harmful effect on strength, immune function, and overall survival.<sup>5</sup> Weight loss provides an important prognostic gauge in the overall survival of the patient. Increased weight loss is inversely proportional to survival time.<sup>1,6</sup> Loss of muscle mass is first noticed over the epaxial, gluteal, scapular, and temporal muscles<sup>7</sup> and is easily detected during a routine physical exam. There does not appear to be a cause and effect relationship between anorexia and cachexia, with weight loss exceeding that expected with simply a decrease in caloric intake.<sup>1</sup>

Cachexia has been seen in animals with cancers, cardiac disease, renal disease, and myriad other serious illnesses and injuries. Loss of 25-50% of the lean body mass compromises the immune system and affects muscle strength, with death resulting from infections, pulmonary failure or both.<sup>8</sup>

### PATHOPHYSIOLOGY

Cancer associated starvation occurs as a consequence of an imbalance between the nutritional needs of the patient, the demands of the tumor and the availability of nutrients in the body.<sup>9,10</sup> The competition for nutrients between the tumor and the host promotes a variety of metabolic disturbances including alterations in carbohydrate, lipid and protein metabolism. Cytokines play a key role as the main humoral and tumor derived factors involved in cancer cachexia and may be responsible for the majority of metabolic changes associated with cancer cachexia. Table 1 summarizes the effects of cytokines on nutrient metabolism in patients with cancer cachexia.<sup>9</sup>

**Table 1.**

CHO	Increased resistance to insulin Increased glucose synthesis Increased Cori cycle activity
Protein	Increased protein breakdown (catabolism) Increased liver (acute phase proteins) and tumor protein synthesis
Lipid	Increased lipid mobilization Elevated levels of triglycerides

### PHASES OF CACHEXIA

There are three phases of cachexia identified in humans; the veterinary profession manages cachexia based on these patterns. Throughout the first phase, the patient does not exhibit any clinical signs; however, the biochemical changes are already occurring. These include elevations seen in lactate levels through the glycolysis

process, an increase in insulin levels, causing peripheral insulin resistance, and alterations in amino acid and lipid profiles.<sup>5</sup>

During the second phase of cachexia, clinical signs can become evident presenting as anorexia, weight loss, and lethargy. Often owners attribute these early signs to the pet's aging process, and thus not recognize the clinical significance. The final phase is characterized by marked loss of body fat and protein stores, severe debilitation, weakness, and biochemical evidence of negative nitrogen balance.<sup>5</sup> If left untreated, cachexia can be the ultimate cause of death.

### THERAPEUTIC STRATEGIES

The optimal therapy is to manage the underlying disease process. In veterinary medicine therapeutic strategies generally include management of anorexia, nutritional support, nutrient supplementation, and the provision of omega-3 fatty acids.

### MANAGING ANOREXIA / HYPOREXIA

Nutritional counseling should be a part of the pretreatment plan for all patients. Veterinary nurses/technicians should help owners understand the importance of measuring caloric intake and should have a sequential plan for maintaining nutritional support throughout the treatment process. This may include simple strategies to increase consumption initially (see table 2) which may progress to assisted feeding if warranted. In a patient with a functional GI tract, enteral feeding is preferred. Strategies for managing anorexia in dogs and cats have been thoroughly reviewed.<sup>11</sup> Table 2 is a brief review of those recommendations.

**Table 2.**

<b>Create ambiance /improve service</b>	Create a quiet comfortable feeding area away from disturbances.
<b>Increase Palatability</b>	
<i>Increase moisture</i>	Switch to canned food / add water to kibble. <b>Caution:</b> some cats may have texture preferences and prefer dry food
<i>Increase fat</i>	Higher fat diets are more energy dense so less food may be required to meet needs.
<i>Increase protein</i>	Dogs may select foods with higher protein level
<i>Sweet and salty</i>	Adding sweet flavor ( <b>No</b> artificial sweeteners) as top dressing may increase palatability for dogs but not cats. Adding salt (if appropriate) may increase palatability for dogs but not cats.
<b>Freshness, aroma, and food temperature</b>	Provide 'fresh' canned / dry foods or home prepared foods. Warming foods to no greater than body temperature may also release aromas.
<b>Rarity</b>	Uncommon or rare food may entice some dogs and cats to eat. Best to offer foods that are uncommon but not completely novel.
<b>Variety</b>	If a variety of options are provided each should be carefully measured to ensure accurate accounting of food intake /preferences. This approach should not be used if food aversions are likely, so that the patient will not develop a learned aversion to all the therapeutic options.
<b>Drug administration</b>	Never top dress food with medication or use the desired diet to administer medication. Avoid giving medications immediately before/ after a meal if possible.
<b>Eliminate physical barriers</b>	Be sure food bowls are accessible and account for any limitations in movement (raise bowls, remove E collars, etc)

<b>Appetite Stimulating drugs</b>	No recommended as effects are unpredictable, intermittent, and short lasting. If above approaches are ineffective assisted feeding is recommended.
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**KEY NUTRITIONAL FACTORS IN THE MANAGEMENT OF CACHEXIA**

While it is not possible to reverse the wasting process with nutritional supplements alone, our patients do need to be fed, and through manipulation of nutrients benefits can be seen in some of the changes the body is undergoing.<sup>1</sup> Proper nutrition can be key to managing cachexia with provision of calories, protein, fat and modulation of cytokine production.<sup>5</sup> Specific dietary recommendation should consider the stage of disease, the patient's energy needs, current and past nutritional status, and ability or willingness to eat.<sup>6</sup>

The caloric distribution in the food should emphasize calories obtained from fats and proteins (rather than carbohydrates) since glucose is the preferred fuel for tumor cells in cancer cachexic patients, and fatty acids and amino acids are not. In cancer cachexia patients, the goal is to feed the patient, and starve the tumor cells. Ideally a food should contain 50-60% of the calories from fat, 30-50% of the calories from protein and the remaining portion from carbohydrates.<sup>6,12</sup>

Omega-3 fatty acids, especially those found in certain types of cold water fish and fish oil (eicosapentaenoic acid [EPA], docosahexaenoic acid [DHA]), are probably the most important nutraceuticals to consider for animals with cancer.<sup>9,12, 13</sup> Studies using animal models have shown that supplementation with EPA and DHA can help to prevent cachexia and metastatic disease processes. These fatty acids obtained from the omega-3 class of fats produce less potent inflammatory mediators than the omega-6 class of fatty acids, which are viewed as pro-inflammatory. When the body uses the omega-3 class of fatty acids to produce cytokines, the inflammatory response produced is decreased in proportion to the level of omega-3 fatty acids in the diet. A recommended a dose of 40 mg/kg of EPA, and 25 mg/kg of DHA. Using the common formulation of most fish oil capsules, to achieve this concentration you would need to provide ~ 1 gram capsule/10# body weight.<sup>5</sup> Many recovery diets already have this incorporated into the diet and additional supplementation is not recommended.

Dietary protein should be highly digestible and go above levels normally used for maintenance of adult animals, due to the catabolic process. Protein levels of 30-50% are recommended, with dogs around 30 to 45% and cats around 40 to 50% DMB. Looking at protein levels another way, the minimum recommend intake is 5.14 grams/100 kcal with 6-7 grams/100 kcal preferred.<sup>5,13</sup>

As stated previously, tumor cells preferentially use glucose for energy. Selecting a carbohydrate with a lower glycemic index would provide a slower release of carbohydrate generated glucose into the blood stream than would those with higher glycemic indexes. Rice is one of the carbohydrates with a highest glycemic index, with barley, sorghum and corn having much lower glycemic indexes.<sup>6</sup>

**FEEDING METHODS**

Enteral feeding is always the preferred delivery method, provided the patient has a functional gastrointestinal tract. Oral feeding of a canned or dry pet food would be the first choice with cachexia patients.<sup>6,12,13</sup> When a patient is unwilling or unable to consume the desired amount of food orally, various feeding tubes can be used. The specific tube selected will vary based on the patient, the desired length of use and the owner's willingness to feed at home. Diet selection would also be based on the route selected for feeding. Preparation of home-cooked diets can be used short term to tempt the patient to eat but should only be used long-term after consultation with a nutritionist. There are also a number of excellent therapeutic diets available that fit the recommended diet profile and can be fed both orally and via tube feeding.

**SUMMARY**

It is essential that veterinary nurses/technicians recognize and understand cachexia and its effect on patients. Additionally, it is vital for healthcare team members to employ nutritional strategies to help manage anorexia and the imbalance between the nutritional needs of the patient and the availability of nutrients in the body. Feeding strategies should be aimed at alleviating the competition for nutrients between the disease process and the host which result in a variety of metabolic disturbances including alterations in carbohydrate, lipid, and protein metabolism. While cachexia is an obvious sign of biochemical imbalances within the body, these changes have been occurring for a while by the time we see the physical changes. Veterinary healthcare team members need to continue to feed patients through disease and cancer treatment. By recognizing changes these disease processes

have caused within the body, a diet recommendation can be used to help the patient instead of the tumor or disease process, thus resulting in more positive outcomes, healthier patients, and happier clients.

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