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Nutritional status of cats with cancer: nutritional evaluation and recommendations

ABBREVIATIONS USED IN THIS CHAPTER

BCS: body condition scoring
CNS: central nervous system
FeLV: feline leukemia virus
MER: maintenance energy requirement
NSAIDs: non-steroidal anti-inflammatory drugs
RER: resting energy requirement
SGA: subjective global assessment

Nutritional status of cats with cancer: nutritional evaluation and recommendations

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The impact of diet on neoplastic disease is multi-faceted. Both dietary habits and nutritional status have been found to be risk factors for the development of certain types of cancer. Nutrition, including special diets and specific nutrients, has also been investigated for its therapeutic role in cancer patients. In addition, the response to chemotherapy and tolerance of treatment has been found to be associated with nutritional status.

With the current lack of nutritional investigation specific to feline cancer patients, the focus of this chapter will be on what we know about the clinical presentation of this population, the process of assessing nutritional status in cats, the significance of poor nutritional status in cats affected with neoplasia, and what strategies we currently have at our disposal to intervene in cancer patients who are experiencing anorexia, weight loss, and a decline in body condition.

The interactions of diet and neoplasia have been much more extensively investigated in human patients, and what preliminary studies exist in veterinary medicine almost all focus on canine cancer patients. Cats, however, do make up a substantial portion of the oncological caseload and one might be tempted to apply findings in other species to the feline patient. This, however, should be done with caution given the many unique aspects of feline physiology, metabolism, and disease. For example, one report found that the minority of canine cancer patients (5%) had an underweight body condition *(Michel et al, 2004)*. Conversely, the clinical impression has been that feline cancer patients are often in poor body condition. A recent investigation at the University of Pennsylvania found this to be the case with 44% of patients assessed as having an underweight body condition and > 90% as having evidence of muscle wasting *(Baez et al, 2007)* **(Figure 1)**.

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Figure 1 *- Over 90% of feline cancer patients examined in an investigation at the University of Pennsylvania were found to have experienced muscle wasting (Baez et al, 2007).*

1 - Characteristics of the feline cancer population

Cats comprise approximately 26% of all cancer patients seen by the oncology service of the University of Pennsylvania and the fraction of cats versus dogs has remained constant over the past decade. Despite the fact that cats represent a significant portion of patients that undergo treatment through the oncology section, there is limited information regarding the feline cancer population on how nutritional factors might influence treatment and outcome. In order to characterize the feline cancer population better in terms of age, breed, sex, body weight, and what types of malignancies they were treated for, information on all cats with malignancies that were seen by all sections of the Veterinary Hospital of the University of Pennsylvania over the past three years was collected. This population may be representative of the feline cancer population in many other larger urban referral centers.

► Epidemiologic data

A total of 712 cats with a diagnosis of various types of cancer were evaluated. Eighty percent were domestic short hair cats, with a slight over-representation of males versus females (52.7 versus 47.3%) of which all but one cat was neutered. The majority of cats were middle-aged to older, with a mean age of 11 years and a mean body weight of 4.58 kg. Sixty percent of the cats had different types of solid tumors and 40% had lymphoma or leukemia. When comparing cats with solid tumors to cats with lymphoma or leukemia, we found that these two groups differed significantly in age and body weight; cats with solid tumors were significantly older and heavier than cats with lymphoma/leukemia with a mean age of 12.0 years versus 10.5 years ($p< 0.0001$) and a mean body weight of 4.7 kg versus 4.4 kg ($p= 0.049$). This difference is not surprising since most cats with lymphoma present with signs of systemic disease and multi-organ involvement at the time of diagnosis.

► Feline lymphoma

Cats with lymphoma represent a significant portion (40%) of the total hospital feline cancer population and an even higher proportion of the oncology section's cat population, since many of these are treated with systemic chemotherapy. The original World Health Organization Classification system listed the various anatomic forms as generalized, alimentary, thymic, skin, leukemia (true, i.e. only blood and bone marrow involved) and others *(Owen, 1980)*. A more simplified and practical classification system includes only 4 groups and feline lymphoma is typically classified according to anatomic site: the thoracic form, the alimentary form, the multicentric form, and an unclassified form (skin, leukemia, CNS, nasal etc) *(Moore et al, 2001)*.

Alimentary lymphoma is the most common anatomic form of lymphoma currently seen in our hospital. This is probably also representative of the situation in most other oncology practices since most cats with lymphoma that are diagnosed today are FeLV negative with primary alimentary involvement. Cranial mediastinal lymphoma typically found in FeLV positive younger outdoor cats is not as common anymore *(Gabor et al, 1998; Vail et al, 1998; Richter, 2003;*

Unlike many dogs, cats with lymphoma are typically diagnosed when they have clinical signs from their lymphoma. Systemic signs secondary to lymphoma will constitute a sub-stage B category, which according to many studies is associated with a worse prognosis. In fact, sub-stage B is a more consistent negative prognostic factor in the canine lymphoma literature than stage of disease *(Valerius et al, 1997; Baskin et al, 2000; Garrett et al, 2002; Simon et al 2006)*.

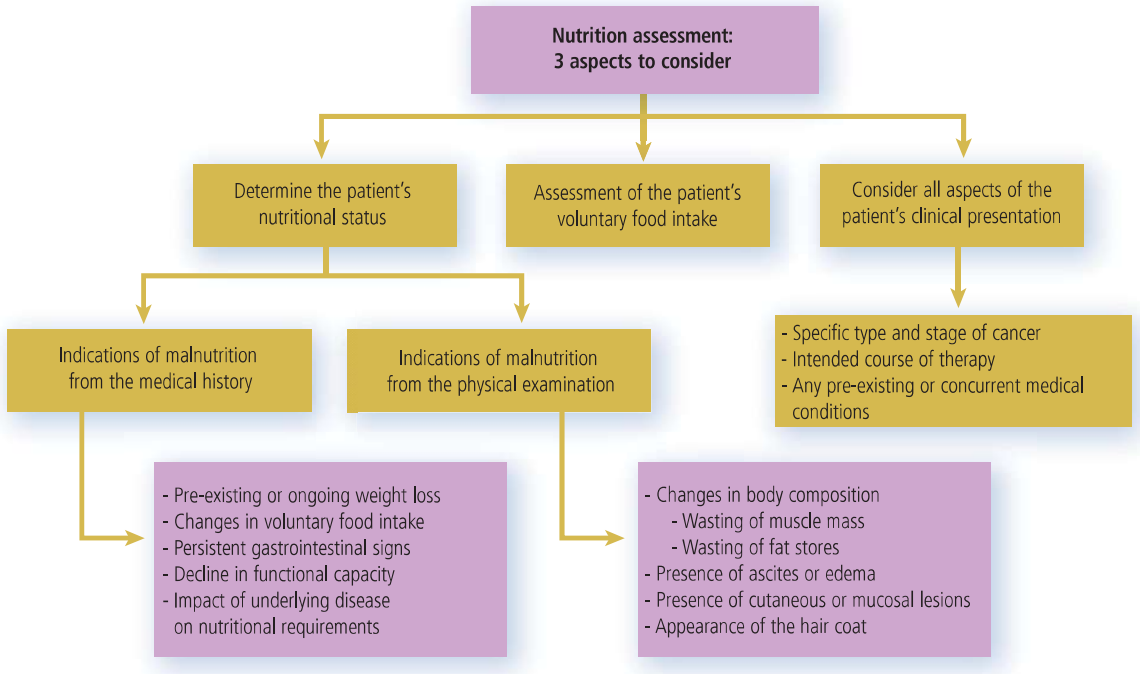
Louwerens et al, 2005; Milner et al, 2005). The alimentary forms of lymphoma often pose a challenge to the clinician both from a therapeutic and a nutritional point of view.

The list of which signs qualify as B-signs has not been completely defined, and leave some room for subjectivity, but in general include any signs of systemic disease at diagnosis, regardless whether these signs are directly associated with the lymphoma, are paraneoplastic, or are from other concurrent illness. Many of these B-signs are typical presenting complaints when cats with lymphoma present for initial evaluation and diagnostics. The typical clinical signs associated with alimentary lymphoma include: decreased appetite, anorexia, vomiting, diarrhea, weight loss and fatigue *(Richter, 2003)*. The clinical signs might have lasted for weeks to months, and many of these cats present in poor nutritional condition. Successful management of these patients requires effective treatment of the underlying malignancy, i.e. chemotherapy, while at the same time controlling nausea, vomiting, diarrhea, anorexia and instituting adequate nutritional support.

2 - Clinical nutritional assessment of cancer patients

The process of nutritional assessment involves evaluation of not only the patient's nutritional status but also the diet it is receiving and how that diet is being fed. Furthermore, this process should not be an initial one time exercise but an on-going practice throughout the patient's course of treatment so that adjustments can be made in diet and feeding recommendations based on the patient's response to therapy. The actual task of nutritional assessment involves several steps **(Figure 2)**. First determine the patient's nutritional status which is a subjective evaluation based on the medical history and physical examination. Next the patient's voluntary food intake should be assessed. Once the patient's nutritional status and food intake have been evaluated, other aspects of the patient's clinical presentation should be considered, including the specific type and stage of cancer, the intended course of

FIGURE 2 - A STEP-BY-STEP APPROACH FOR THE NUTRITIONAL ASSESSMENT OF FELINE CANCER PATIENTS



therapy, and whether or not there are any pre-existing or concurrent medical conditions. Formulating a suitable nutritional plan for each patient needs to encompass all of this information.

The nutritional assessment will help determine whether the patient is experiencing malnutrition or at risk of becoming malnourished, whether the diet and the intake of that diet are adequate to the patient's nutritional needs, whether any specific dietary management, including assisted feeding, is indicated and, in the case of assisted feeding, which route of feeding will be the safest, most effective and best tolerated by the patient. The process of nutritional assessment can also identify potential problems that might arise as a consequence of the dietary management, and allow for planning to prevent them or anticipate them through appropriate monitoring.

► Determining nutritional status

A technique referred to as subjective global assessment (SGA) was developed for the nutritional assessment of human patients approximately 20 years ago *(Detskey et al, 1987)*. The technique was designed to utilize readily available historical and physical parameters in order to identify malnourished patients who are at increased risk for complications and who will presumably benefit from nutritional intervention. The assessment involves determining:
- whether nutrient assimilation has been restricted because of decreased food intake, maldigestion or malabsorption;
- whether any effects of malnutrition on organ function and body composition are evident;
- and whether the patient's disease process influences its nutrient requirements.

To adapt the SGA to cancer patients, the medical history should be assessed in five areas:
- pre-existing or ongoing weight loss
- extent of voluntary dietary intake
- the presence of persistent gastrointestinal signs either from the primary disease or treatment the patient is receiving
- the patient's functional capacity (e.g., weakness, presence of exercise intolerance)
- and the impact of the patient's underlying disease state.

When dealing with cancer patients one must consider the ways in which the tumor could directly or indirectly affect food intake, the impact that cancer therapy may have on food intake and metabolism, and the recognition that the tumor itself may exert effects on metabolism that negatively influence nutritional status.

It is often difficult to document a history of weight lost since most animals are only weighed when they come in to a veterinary clinic and not always then. It is critical that cats being treated for cancer are weighed consistently on the same scale and that the scale is sensitive and accurate for animals in the feline weight range. It is also important to know the time course over which the weight loss has occurred. Rapid weight loss is generally of greater concern because it is more likely to involve a greater percentage of lean tissue catabolism than a more gradual weight loss. Having said that, cancer cachexia syndrome, as documented in human cancer patients is characterized by loss of both lean body mass and adipose tissue and can take a chronic course.

The physical examination focuses on changes in body composition, specifically wasting of fat stores and muscle mass, the presence of edema or ascites, the presence of mucosal or cutaneous lesions, and the appearance of the patient's hair coat. Several excellent body condition scoring systems (BCS) have been developed for cats *(Laflamme, 1997; German et al, 2006)*. However, these systems do not apply well to cats with cancer because they depict patients that deviate from optimal based on under- or overconsumption of protein and calories. It has been reported in a study from the University of Pennsylvania that over 90% of cats diagnosed with cancer have evidence of muscle wasting even in cases where the patient had adequate or even excessive fat stores *(Baez et al, 2007)*. Without careful examination, which involves palpation of skeletal muscle mass over bony prominences (such as the scapulae or vertebral column), some of these patients might be misclassified as overweight

Regardless of the reason a cat is presented at the clinic, the body weight must be recorded.

Figure 3 - Evaluation of the cat's body composition.

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Feline cancer patients can present with a relatively normal body silhouette and weight.

Hence, body condition scoring requires manual palpation to assess both fat and lean body mass.

Assessment of body fat in cats should always involve palpation of the abdominal fat pad, in addition to palpation over the rib cage.

In addition to the standard techniques used for body condition scoring, feline cancer patients should always be assessed for evidence of muscle wasting by palpation for muscle mass over boney prominences such as the vertebral spinous processes.

TABLE 1 - MUSCLE MASS SCORING SYSTEM

Score	Muscle Mass
0	Severe muscle wasting as evidenced by pronounced decreased muscle mass palpable over the scapulae, skull, or wings of the ilia.
1	Moderate muscle wasting as evidenced by clearly discernable decreased muscle mass palpable over the scapulae, skull, or wings of the ilia.
2	Mild muscle wasting as evidenced by slight but discernible decreased muscle mass palpable over the scapulae, skull, or wings of the ilia.
3	Normal muscle mass palpable over the scapulae, skull, or wings of the ilia.

or even obese **(Figure 3)**. Thus we recommend subjectively evaluating muscle mass **(Table 1)** in addition to using one of the standard body condition scoring systems available.

The findings of the historical and physical assessment are used to categorize the patient as:
A: well nourished
B: borderline or at risk of becoming malnourished
C: significantly malnourished.

Coupling this assessment with the patient's cancer diagnosis, stage, treatment protocol, and prognosis will aid in making decisions about nutritional therapy.

► Assessment of voluntary food intake

In order to be able to assess whether that patient's food intake is adequate, you must have a caloric goal, select an appropriate food, and formulate a feeding recommendation for the patient. By doing so, you will have an accurate account of how much food is offered to the patient, and will be able to evaluate the patient's intake based on how much of the food is consumed.

> Hospitalized patients

For hospitalized patients, we recommend using an estimate of resting energy requirement (RER) as your initial caloric goal **(Table 2)** as most hospitalized patients are not expending much more energy than RER while they are caged. Under such conditions most patients eating at least RER will

lose little if any weight. Clearly if a patient is willing to consume calories in excess of RER it should be permitted to do so. However, starting out with this amount of food will provide a goal to aim for with patients who have a decreased appetite. It is critical to monitor both the patient's food intake and body weight to establish whether the patient is in energy balance or not and to permit timely adjustment of the dietary plan if the patient is not responding as anticipated **(see chapter 13)**

> Out-patients

The majority of cancer patients are treated as out-patients and therefore will require additional caloric intake to compensate for energy expended on voluntary physical activity. Under these circumstances, the daily maintenance energy requirement (MER) should be estimated **(Table 3)** and used to calculate the initial caloric goal.

This information should be converted into clear feeding directions for the cat's caregiver using specific portions of whichever foods are being offered to the patient in a manner analogous to how a drug dosage would be calculated and prescribed. There should be a plan for reporting back to the clinician about daily food intake and for accurately monitoring body weight on a regular basis to assess the patient's response and allow for modification of the feeding plan as appropriate.

TABLE 2 - ESTIMATION OF RESTING ENERGY REQUIREMENT (RER)

RER = 70 BW(kg)$^{0.73}$
or RER = 30 BW(kg) + 70*

BW (kg)	RER = 70 BW(kg)$^{0.73}$
1	70
1.5	94
2	116
2.5	137
3	156
3.5	175
4	193
4.5	210
5	227
5.5	243
6	259
6.5	274
7	290
7.5	305
8	319

**patients weighing >2 kg*
[For patients with excessive adipose tissue use a conservative estimate of the individual's lean body weight for the calculation.]
BW: body weight

TABLE 3 - ESTIMATION OF DAILY MAINTENANCE ENERGY REQUIREMENT (MER)

MER = 1.1 to 1.2 x RER

BW (kg)	1.1 x RER (kcal)	1.2 x RER (kcal)
1	77	84
1.5	103	113
2	128	139
2.5	151	164
3	172	187
3.5	193	210
4	212	232
4.5	231	252
5	250	272
5.5	267	292
6	285	311
6.5	301	329
7	319	348
7.5	336	366
8	351	383

Figure 4 - Assessment of weight loss. *Many feline cancer patients have already experienced weight loss at the time of diagnosis and are at risk of further deterioration in body condition during the induction phase of chemotherapy.*

► Determining the need for assisted feeding

Patients who are unable to eat or whose voluntary food intake is insufficient to maintain energy balance will require some form of intervention whether it is as simple as coax feeding or a more aggressive approach using some form of assisted feeding **(see chapter 13)**. Clearly the feeding management of those patients who are already significantly malnourished at the time of presentation should receive immediate attention.

It is often the case that reduced food intake as a consequence of cancer therapy can be anticipated. Therefore a plan should be in place for nutritional intervention should the need arise, particularly in the case of patients whose nutritional status is considered borderline at the commencement of therapy.

3 - Cancer cachexia syndrome

► Distinction between weight loss due to starvation and cachexia

It is well recognized that weight loss is a common finding in human cancer patients and one which has been shown to have associations with clinical outcome *(Tisdale, 1997)*. As already stated, weight loss in association with neoplasia can occur for a number of reasons including the effects of the tumor and the cancer therapy. However, the weight loss seen in many human cancer patients does not appear to be attributable to decreased food intake alone. In simple starvation, individuals lose principally adipose tissue, whereas patients with neoplasia can experience loss of both lean and adipose tissues *(Moley et al, 1987)*. Furthermore, the magnitude of the weight lost often does not correspond to the amount of food consumed, and this weight loss cannot be reversed by a concomitant increase in caloric intake *(Costa et al, 1980)*.

This paraneoplastic syndrome of cancer cachexia is hypothesized to result from metabolic alterations that exist as a consequence of the underlying tumor. Derangements in carbohydrate, lipid, and protein metabolism have been found in both human and canine cancer patients that may contribute to weight loss *(Shapot & Blinov, 1974; Nixon et al, 1980; Nolop et al, 1987; Shaw & Wolfe, 1987; Vail et al, 1990; Tayek, 1992; McMillan et al, 1994; Ogilvie et al, 1994;1997; Vail et al, 1994; Dworzak et al 1998)*. There is also evidence that cytokines, including TNFα, IL-1, and IL-6, could play a role in these metabolic alterations *(Gelin et al, 1991; Moldawer and Copeland, 1997)*.

What remains unknown is to what extent the weight loss seen in feline cancer patients is attributable to decreased appetite or the direct effects of the tumor or therapy on nutrient assimilation or metabolism and to what extent cancer cachexia syndrome **(Figure 4)** may be responsible. This is important because in the former situation careful attention to feeding management should be able to avert or ameliorate loss of weight and body condition, whereas in the latter situation, effective means of counteracting the progression of cachexia remain elusive.

► Body condition as a prognostic factor

Cancer cachexia syndrome has been implicated as a negative prognostic factor for survival, surgical risk, response to chemotherapy, and tolerance of treatment in human cancer medicine *(Daly et al, 1979; DeWys et al, 1980; McCaw, 1989)*. There have been some preliminary studies in companion animal cancer patients looking at body condition and weight loss. When body condition was evaluated in dogs seen at the oncology service at the University of Pennsylvania only 5% of the dogs were considered significantly underweight with a BCS <2.5/5 (1= cachectic, 3=optimal; 5=obese) while 29% were classified as significantly overweight (>4/5) *(Michel et al, 2004)*.

Conversely, an investigation of feline cancer patients at the same institution documented that up to 44% of cats with cancer treated through the oncology service had a BCS <3/5 *(Baez et al, 2007)*.

This study also found that both a low BCS as well as a low body weight had a negative impact on prognosis. Both cats with solid tumors and cats with lymphoma have significantly shorter survival times if their BCS or their body weight were low. Furthermore, a positive correlation between remission status and BCS was found.

Cats in remission are more likely to weigh more and have a higher body condition score.

The presence of weight loss or cachexia was not found to be an independent negative prognostic indicator as it has been in similar studies in human oncology *(Vigano et al, 2000)*. Nevertheless, the results suggest that weight loss and deterioration of body condition are significant problems in feline cancer medicine and may have consequences for response to treatment, remission duration and quality of life.

4 - Nutritional consequences of anti-cancer therapy

Debilitated cats with advanced alimentary lymphoma represent some of the most challenging cases in medical oncology. The poor nutritional status in these patients is typically a result of a combination of factors resulting in prolonged inadequate nutrition. These signs may be direct effects of gastrointestinal involvement, stage of disease or may also, in part, be due to a deranged metabolic state secondary to cancer cachexia syndrome.

► Secondary effects of chemotherapeutic protocols

Regardless of the pathogenesis, in order to reverse these signs, treatment of the underlying malignancy is necessary. This requires the use of chemotherapy. The choice of chemotherapeutic protocol is influenced by cell type or lymphoma grade. Most oncologists use a combination of chemotherapeutic drugs including, prednisone, asparaginase, vincristine, cyclophosphamide, methotrexate, and doxorubicin to treat cats with intermediate to high grade lymphoma (intermediate to large cell type) *(Moore et al, 1996; Valerius et al, 1997; Vail et al, 1998; Zwahlen et al, 1998; Krystal et al, 2001; Teske et al, 2002; Richter, 2003; Milner et al, 2005)*. Many of these drugs are associated with gastrointestinal signs such as nausea, vomiting, anorexia, diarrhea, and fatigue; clinical signs which many of these cats already exhibit. Debilitated patients may be more likely to experience adverse reactions to treatment, require dose reductions, have a decreased response to treatment and have a worse outcome. The induction phase can be particularly difficult and requires careful monitoring of tumor response, addressing toxicity from treatment as needed and constant assessment of the general status of the cat.

A cat with alimentary lymphoma and severe weight loss.

► Variability of individual responses

Lymphoma is a chemotherapy-responsive malignancy and some cats with high grade lymphoma may go into remission quickly, tolerate the chemotherapy and improve without specific nutritional intervention. However, others may take longer to respond and/or become increasingly intolerant to chemotherapy and suffer progressive weight loss through the induction phase. Some of these cats may never attain remission and fail early, and others may be taken off chemotherapy prematurely due to unacceptable toxicity and poor quality of life. These cats require intervention.

Dietary aversion

If a food is associated with distress, an unpleasant experience (hospitalization) or digestive problem (poisoning), the food is likely to be avoided in the future. This phenomenon is known as aversion. Aversion is a form of negative conditioning used by animals to avoid foods that are unsuitable for them.

In cats, aversion sets in very quickly. A single meal associated with unpleasantness leads to a refusal to eat. Such aversion can persist for at least 40 days *(Bradshaw et al, 1996)*. The smell alone of a food associated with digestive disorders is enough to elicit aversion. Cats even go so far as to show aversion for their usual food if it is served in the presence of an air current bearing the odor of a food to which they have developed an aversion.

Table 4 - Signs of learned food aversion

The patient initially shows interest in food when it is offered but backs away after smelling or tasting the food.
The patient salivates, swallows repeatedly or turns its head away when food is offered.
A caged patient positions itself as far away as possible from the feeding bowl.

A prospective study on the incidence of toxicity and overall quality of life in dogs and cats treated with chemotherapy at the University of Pennsylvania confirmed that weight loss, vomiting, and anorexia were more common in cats than dogs *(Bachman et al, 2000)*. Sixty percent of the cats lost weight in the induction phase, this is in sharp contrast to the situation in dogs, where close to 70% gained weight (p = 0.0077). Doxorubicin was the drug most often associated with weight loss and vomiting in both cats and dogs. These results reflect the complexity of the situation. Chemotherapy is necessary to treat the underlying malignancy, yet it may also exacerbate the clinical signs and contribute to further weight loss, vomiting, diarrhea and reduced quality of life. The overall median survival of cats with lymphoma is less than one year; poor nutritional status and low body weight are associated with worse outcome in cats *(Baez et al, 2007)*. It is unknown whether early intervention to reverse the loss of weight and body condition improve outcome in these cats, but these results clearly show that more attention should be paid to ensuring adequate nutritional support, both to improve quality of life as well as to potentially prolong survival.

5 - Dietary intervention

► Coax feeding

When a cat exhibits a decreased appetite it is natural to try to tempt it to eat by offering a variety of palatable foods. Very often the caregiver will further attempt to coax the patient to eat by putting the food close to the cat's face or actually placing food in its mouth. Sometimes these techniques can be successful and lead to adequate food intake by the patient. However, such efforts are labor intensive and time consuming. A feeding plan with specific caloric goals should be formulated in advance so the caregiver can assess the adequacy of the patient's food intake. Furthermore, it is very important to recognize that cats sometimes associate nausea, general indisposition, or pain with the act of eating or even the sight or scent of food. This is called learned food aversion and can further complicate achieving adequate food intake in a patient.

Therefore, whenever attempting to coax feed a cat, one must remain alert to the signs of food aversion **(Table 4)** and recognize that there will be circumstances when it will be necessary to resort to assisted feeding for a time because of the risk of causing or exacerbating this condition. **Table 5** lists some general guidelines on how to approach these patients. However, every patient will be different and it is necessary to observe each individual's behavior in order to decide how best to proceed.

► Assisted feeding

Much of the information gleaned in your nutritional assessment will aid in making the choice of the best route for assisted feeding access. Other information to evaluate in the decision making process should include:

- assessment of gastrointestinal tract function
- assessment of other organ systems that may have an impact on the patient's ability to tolerate specific nutrients
- assessment of the patient's ability to tolerate a feeding tube and tube placement
- assessment of the patient's risk for pulmonary aspiration.

If parenteral nutrition is contemplated, it is also necessary to include assessment of the ability to obtain vascular access and the patient's fluid tolerance.

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Figure 5 - Assisted feeding by esophagostomy tube. *Esophagostomy tubes are relatively non-invasive and simple to place and provide well-tolerated access for assisted feeding in feline patients.*

There are some additional considerations to take into account when assessing cancer patients for assisted feeding. Certain chemotherapeutic agents can impair wound healing with the consequence of a greater risk of septic complications with tubes that are placed into the peritoneal cavity (e.g. gastrostomy and enterostomy tubes). This risk can be magnified if the patient is receiving immunosuppressive drugs. Radiation therapy can have similar consequences if the tube placement is within the field of treatment. The esophagostomy tube has many of the advantages of a gastrostomy tube but carries a lower risk of serious

septic complications (**Figure 5**). These tubes are simple and inexpensive to place and usually well-tolerated by feline patients.
One final consideration is the fact that assisted feeding is a form of life-support. Used properly it could have the benefit of both prolonging life and ensuring a better quality of life for the patient. However, there may be circumstances, in terminal patients, where humane euthanasia is in the better interest of the patient then prolonging life. It is often more difficult for involved pet owners to terminate life supporting therapies than to initiate them and therefore the decision to use assisted feeding in a patient should bear in mind these ethical issues.

Figure 6 is a decision tree that illustrates how these various factors should be taken into account to choose the safest and most effective route of assisted feeding. Assisted feeding in feline patients is covered in more detail in chapter 13.

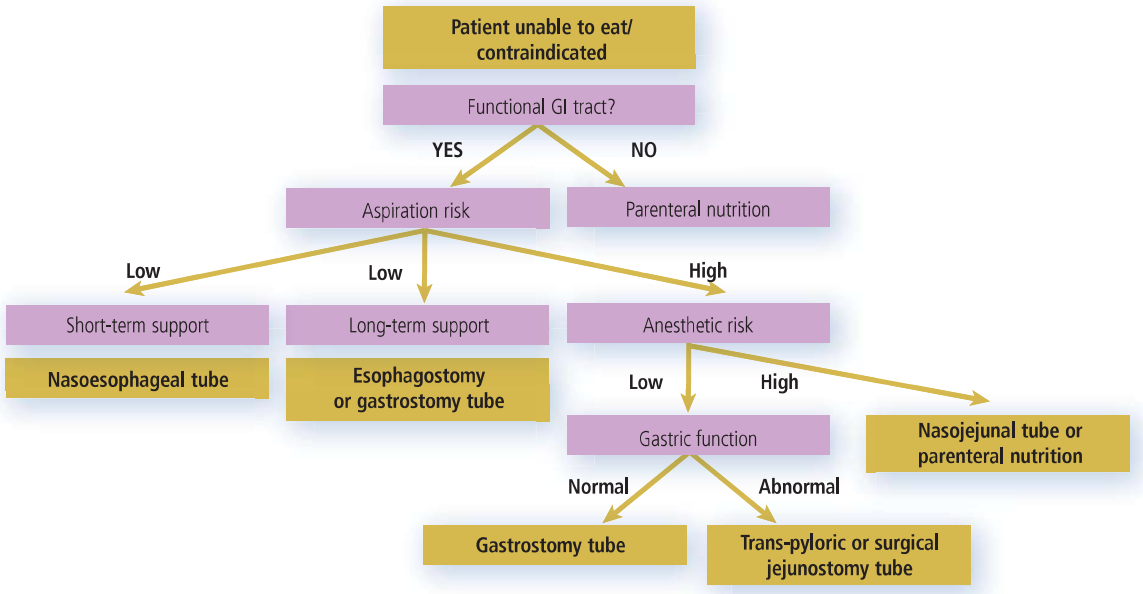
► Diet selection

In general, diet selection is based on which of patient's problems can and should be addressed with nutrition and the nutritional requirements of the patient. While there have been many investigations of ways in

TABLE 5 - GUIDELINES FOR COAX FEEDING

Resist the temptation to coax a cat to eat when it is showing overt signs of nausea and discomfort. Cats that gulp or salivate at the sight or scent of food, who turn their heads away from the food or spit it out when it is placed in their mouths should not have food forced on them.
Consider the possibility of using anti-emetic drugs if vomiting and nausea are a problem.
Consider the use of assisted feeding as an alternative.
Consider appetite stimulant drugs; however, these should only be used in patients that either have no signs of food aversion or who have begun to feel better and may now be able to overcome a food aversion.
For cats that are showing some interest in food: - try novel food items. Remember that table foods will not provide all of the nutrients that a cat requires and if a cat eats an exclusively home cooked diet for more than a few days, that diet should be evaluated by a veterinary nutritionist for nutritional adequacy; - make mealtimes as comfortable and unstressful as possible. Try not to schedule them at the same time as other treatments such as the administration of medications; - divide the day's food into as many small meals as possible. Offering small meals of fresh food is more likely to meet with success than a few large meals no matter how tempting the food is; - the food ingredients that increase palatability for most cats include moisture, fat, and protein. Switching from a dry pet food to a canned food or the other way around may improve food acceptance; - remember that "mouth feel" (the texture and consistency of food) is an important aspect of palatability for cats (so switching to canned foods will not always meet with success).
Trying foods with increased fat or protein content should be done with consideration of the patient's tolerance for these nutrients.
The standard advice for getting anorexic cats to eat has been to warm the food to just below body temperature. This is believed to increase the aroma of the food, which in turn will enhance the taste. However, this might be counterproductive in patients that are showing food aversion.

FIGURE 6 - DECISION TREE TO DETERMINE THE ROUTE OF ASSISTED FEEDING



which diet and specific nutrients may be used to slow or antagonize tumor growth, modulate immune function, or counteract the cancer cachexia syndrome, most of this research has been done in rodent models or human patients. There have been preliminary clinical investigations involving canine cancer patients, but none to date that have involved cats. A canned low carbohydrate diet that was fortified with fish oil and arginine was found to increase survival time and disease free interval in dogs with stage III lymphoma *(Ogilvie et al, 2000)*. With the exception of the additional fish oil, many conventional canned cat foods have a similar formulation to the diet that was used in this investigation.

The major consideration for diet selection for cats with cancer should be acceptance by the patient. The diet should meet feline nutritional requirements and if it does not, it should be supplemented to address any deficiencies. Ideally, the diet should be of high caloric density, as this will aid in ensuring sufficient energy intake by the patient, especially in cases when appetite is decreased. In addition, if the patient has clinical signs or disease secondary to or in addition to cancer that would benefit from dietary management, efforts should be made to select and feed a diet formulated to address those conditions.

Lastly, in patients with alimentary neoplasia, in particular lymphoma, nutrient malabsorption can occur. While this can lead to generalized protein-calorie malnutrition, it can also lead to specific micronutrient deficiencies. One nutrient deficiency which has been reported in cats with gastrointestinal disease, including lymphoma, is cobalamin deficiency *(Simpson et al, 2001)*. Cats with inflammatory bowel disease complicated by cobalamin deficiency have shown improved weight gain and response to therapy with parenteral supplementation of this vitamin (cobalamin, 250 µg SC once weekly, for 4 weeks) *(Ruaux et al, 2005)*. It is our clinical impression that cats with alimentary lymphoma also can benefit from parenteral cobalamin supplementation.

6 - Pharmacological intervention

In addition to treating the underlying malignancy with surgery, radiation therapy, chemotherapy or a combination of these modalities, additional medications may be indicated and necessary to reverse weight loss and improve quality of life. In order to choose the most effective drugs and provide the optimal care for the individual patient it is important to determine the cause for the inadequate food intake and weight loss.

► Causes of dysorexia and anorexia

Anorexia is the failure of the usual appetite signals and can be a direct or indirect effect of the cancer itself or the cancer treatment, specifically chemotherapy. Decreased or loss of appetite may be a direct result of abdominal pain or discomfort, and early satiety due to restricted gastric accommodation or delayed emptying secondary to tumor infiltrate. Primary intestinal tumors may lead to complete or incomplete obstruction, ileus, malabsorption, diarrhea or constipation which again can lead to discomfort, bloating, anorexia or nausea *(Uomo et al, 2006)*.

Chemotherapy may contribute to further decreasing appetite by its effects on the vomiting center as well as the effect on the gastrointestinal tract. Certain chemotherapeutic drugs such as vincristine can cause ileus and constipation, which again may feed into the cycle of anorexia and depression *(Ogilvie et al, 2001)*. The direct cytotoxic effects on the intestinal epithelial lining may lead to sloughing and make possible bacterial translocation and secondary intestinal bacterial overgrowth.

Chemotherapy induced gastroenteritis can induce nausea, vomiting and diarrhea. The risk for sepsis is especially important if the patient experiences concurrent myelosuppression. If there is a potential for sepsis, broad-spectrum antibiotics with good gram positive and gram negative coverage are indicated in these patients.

► Analgesia

Pain and discomfort may contribute to anorexia and weight loss. It is often difficult to determine whether veterinary patients are in pain, especially visceral pain. Visceral pain is commonly reported in human cancer patients with abdominal organ cancer, especially pancreatic cancer. Cancer cachexia is more common in pancreatic cancer than in any other cancer type and up to 80% of the patients are reported to be cachetic *(Splinter, 1992; Ryan et al, 1998)*. Pain medications are routinely provided to palliate these patients *(Li et al, 2004)*.

It is feasible that cats with alimentary lymphoma experience some degree of discomfort or pain, however, the effectiveness of pain medications in improving appetite and reversing the cycle of weight loss in these patients has not been evaluated, and pain medications may not be routinely prescribed. Pain is easier to recognize and therefore more likely to be treated in cats with visible non-resectable solid tumors that invade or destroy bone or that compress nerves. Palliative care with the focus of treating the cancer pain with oral or parenteral pain medication and/or palliative radiation therapy is routinely offered to cats with oral squamous cell carcinoma or osteosarcomas. It is the authors' subjective impression that some of these cats improve and increase their voluntary food intake with such measures. However, there are no studies to confirm these observations.

► Anti-inflammatory drugs

The systemic effects of cancer and metabolic changes associated with cancer cachexia syndrome are mediated by a complex network of pro-inflammatory cytokines *(Jatoi et al, 2001; Walker, 2001)*. Anti-inflammatory drugs may therefore have a role in reversing some of these effects. Non-steroidal anti-inflammatory drugs (NSAIDs) include several different drugs with anti-cycloxogenase activity. These drugs have both analgesic and well as anti-inflammatory effects, and may therefore provide dual benefits to patients suffering from a painful non-resectable tumor and/or the systemic inflammatory effects of the tumor and cancer cachexia syndrome. In addition, the effects against cycloxogenase-2 may have direct anti-cancer effects, especially in tumors over-expressing this enzyme. The direct anti-cancer affects of NSAIDs have been reported only in dogs at this point *(Schmidt et al, 2001; Knapp et al, 2002; Mustaers et al, 2003; Mohammed et al, 2004; Mustaers et al, 2005)*. NSAIDs have been reported to improve some of the symptoms associated with cancer cachexia syndrome and improve quality of life in human pancreatic and other gastrointestinal cancer patients *(Wigmore et al, 1995; McMillian et al, 1997; McMillian et al, 1999)*.

► Appetite stimulating drugs

The use of appetite stimulating drugs and anti-depressants may also be indicated in some patients. It can be very difficult and often impossible to distinguish between anorexia resulting from nausea and anorexia as part of the cancer cachexia syndrome. Therefore anti-emetics should always be considered first or in conjunction with drugs to stimulate appetite. Administering appetite stimulating drugs without providing effective anti-emetics may worsen nausea and cause more vomiting with the potential of creating a learned food aversion. It is also important to rule out and treat any physical causes of nausea, vomiting and subsequent anorexia such as gastrointestinal tumors, intestinal obstruction or chemotherapy-induced gastroenteritis prior to prescribing appetite stimulating drugs.

Megestrol acetate is effective in feline cancer patients and used to improve appetite and promote weight gain.

Megestrol acetate is the most effective and commonly prescribed drug to combat weight loss and cachexia in human oncology. A large meta-analysis found that cancer patients receiving megestrol acetate were significantly more likely to gain or maintain weight than those who did not receive the drug (*Berenstein et al, 2005*). The exact mechanism of action of megestrol acetate is complex and thought to involve stimulation of appetite by both direct and indirect pathways as well as antagonism of the metabolic effects on the principal catabolic cytokines (*Uomo et al, 2006*). Megestrol acetate is also effective in feline cancer patients and used to improve appetite and promote weight gain.

However, **corticosteroids** are used more commonly in the USA, especially in feline lymphoma. Corticosteroids are part of the chemotherapy protocol for lymphoma and used for their cytotoxic effects, however, corticosteroids have additional benefits including appetite stimulation and anti-inflammatory effects which might be beneficial in combating the cancer cachexia syndrome.

Cyproheptadine, an anti-serotonergic, is another appetite stimulant used relatively frequently in cats and still favored by many veterinarians despite the fact that prospective trials in human cancer patients found no improvement in nutritional status in patients receiving cyproheptadine versus placebo (*Kardinal et al, 1990*).

Appetite stimulating drugs are often used in conjunction with other palliative measures in cats. Some seem to benefit from these measures, but it may be impossible to determine which of the palliative drugs is indeed effective in patients where many different strategies to improve appetite are instituted simultaneously; the improvement may in fact be a result of synergistic or complimentary additive effects of a combination of drugs. A combination of drugs or a multimodality approach may indeed be necessary to maintain weight or reverse weight loss.

Nevertheless, it is important to assess all of the above potential contributing factors, i.e. tumor stage and direct gastrointestinal involvement, presence of nausea, pain or discomfort, chemotherapy induced gastroenteritis, or the presence of the cancer cachexia syndrome, so that the most appropriate drugs or drug combinations are administered. There may be a practical limitation to how many different oral medications a cat will tolerate, and forceful administration of excessive unnecessary medications may make the situation worse. **Tables 6** and **7** include drugs with recommended dosages used to decrease nausea, stimulate appetite, improve nutritional status and combat weight loss in cats with cancer.

TABLE 6 - ANTI-EMETIC DRUGS

Drug	Dosage	Comments
Metoclopramide	0.2-0.4 mg/kg [0.1-0.2 mg/lb], SC or PO q6-8 1-2 mg/kg/day [0.5-1 mg/lb], IV CRI	Promotes gastric emptying and acts centrally on the chemoreceptor trigger zone (central effects are less potent in the cat than in other species)
Prochlorperazine	0.1-0.5 mg/kg [0.05-0.2 mg/lb], SC or IM q6-8	Sedative and hypotensive effects (adrenergic antagonist) acts centrally on the vomiting center and chemoreceptor trigger zone
Dolasetron Mesylate Ondansetron	0.5-1.0 mg/kg [0.2-0.5 mg/lb], IV or PO q24 0.3-1.0 mg/kg [0.1-0.5 mg/lb], PO q 24 hr	Acts centrally on the chemoreceptor trigger zone
Dexamethazone	1-3 mg/cat (given as a single dose in conjunction with other anti-emetics)	Unknown mechanism of action; potentates the effect of other anti-emetics

The licensing arrangements for therapeutic agents varies worldwide. Some of these agents may not be licensed or approved for use in cats.

Table 7 - Appetite stimulant drugs		
Drug	Dosage	Comments
Benzodiazepine Derivatives* Diazepam Oxazepam	0.2 mg/kg [0.1 mg/lb], IV 0.5 mg/kg [0.2 mg/lb], PO q12-24	Causes sedation Contraindicated in cats with hepatic failure Effects wane with time when used in sick animals
Cyproheptadine*	0.2-0.5 mg/kg [0.1-0.2 mg/lb], PO q12	Anti-serotonergic Can cause excitability, aggression and vomiting
Megestrol Acetate	0.25-0.5 mg/kg [0.1-0.2 mg/lb], q 24 hr for 3-5 days, then q 48-72 hr	Stimulates appetite by direct and indirect pathways Antagonistic effects on the principal catabolic cytokines Diabetogenic
Prednisone	0.5-1.0 mg/kg [0.2-0.5 mg/lb], q 24	Direct central effects Inhibition of tumor and host-induced substances Direct cytotoxic effects in lymphoma

* *Both the benzodiazepine derivatives and cyproheptadine cause only a momentary increase in appetite and are unreliable for ensuring adequate caloric intake.*

The licensing arrangements for therapeutic agents varies worldwide. Some of these agents may not be licensed or approved for use in cats.

Conclusion

The primary goals of cancer therapy are to prolong life and maintain a good quality of life. Ensuring adequate nutrition is a requirement for both goals to be fulfilled. Human cancer studies have found that cachectic patients have a worse outcome, more complications and a lower response to therapy. The situation is likely similar in cats, as illustrated by one recently published investigation, where:

- remission was positively correlated with a higher BCS
- cats with solid tumors and lymphoma that had an underweight body condition had significantly shorter survival times than cats with a higher BCS *(Baez et al, 2007)*.

Weight loss and the associated reduced quality of life may not only have a negative impact on treatment, but may also have direct consequences for survival, because it may lead to a decision to euthanize. The ability, interest, and willingness to eat voluntarily are major components of having a good quality of life. Most owners and veterinarians will likely agree that a cat that does not eat voluntarily or adequately over long periods of time may not feel well and may be suffering.

Therefore, providing effective nutritional support and offering the appropriate palliative medications to decrease nausea, improve appetite and facilitate voluntary food intake become crucial for prolonging survival. On our service we have found that the majority of cats with lymphoma lose weight in the induction phase of chemotherapy *(Bachman et al, 2000)*. A significant proportion of cats with lymphoma die or are euthanized within the first months of starting chemotherapy. These facts suggest that more focus should be directed towards ensuring adequate nutrition and preventing weight loss in these patients. Early nutritional intervention may not only improve quality of life in cats with cancer but may also have positive impact on survival.

Frequently asked questions

Q	A
How do we know whether it is the treatment or the cancer itself that makes the cat appear nauseated and have a reduced appetite?	This is probably one of the most frequently asked questions by both veterinarians and owners. In order to answer this it is necessary to re-assess the remission status of the cat and to perform a thorough review of the previous treatment history in order to determine whether there is a pattern to the weight loss or whether the nausea might be associated with certain chemotherapeutic drugs. This may require performing an abdominal ultrasound in cats with gastro-intestinal lymphoma and comparing the findings to the pre-treatment staging ultrasound. If the results suggest improvement or even clinical remission, the suspicion is that it is the chemotherapy that is the culprit. If this is the case, giving the cat a short break from treatment may result in a resolution of the problem. Continued chemotherapy should be initiated carefully with prophylactic anti-emetics and dose-reductions should also be considered. If the ultrasound shows persistent lymphoma or even worsening status, other chemotherapeutic drugs with concomitant anti-emetics may be needed.
Is my cat suffering because it is not eating?	It is reasonable to assume that a cat that does not eat does not feel well. There is a gradual scale from not "feeling well" to suffering. A temporary decrease in appetite or even anorexia may be acceptable in most owners' and veterinarians' opinion as long as it is assumed that it does not significantly impact on or interfere with other aspects of the cat's life. However, severe prolonged anorexia and weight loss secondary to any terminal disease for which there is no treatment or palliation is a clear sign of an unacceptable quality of life.
What can I do to improve my cat's food intake?	Appetite is affected by many internal and external signals. Many cancer patients may experience a reduction in appetite due to direct or indirect effects of the tumor and the treatment they are undergoing. Every effort should be made to optimize the patient's wellbeing including addressing conditions such as dehydration, fever, pain, and nausea. Make feeding times as unstressful as possible. Try offering small amounts of a variety of tempting foods but be alert for signs of learned food aversion. Offering many small meals through out the day may meet with more success than fewer larger meals. Sometimes warming the food to body temperature will increase its appeal.
My cat's appetite is very poor and he is losing weight despite a good response to chemotherapy. I have been told a feeding tube could help him through this period but I am concerned about the impact this would have on his quality of life.	Tube feeding is well-tolerated by many feline patients. Esophagostomy tubes, in particular, seem to cause little discomfort to the patient and provide access that permits the feeding of canned cat foods. Tube feeding is not possible in patients that have uncontrolled vomiting. However, when these conditions are not present or are properly managed, tube feeding will improve the patient's nutritional status, energy level, and overall sense of well-being. Since the cat is in remission but still losing weight, the weight loss may be due to chemotherapy induced nausea and fatigue, minor dose reductions and effective anti-emetics should also be considered in addition to feeding tube placement.

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