Weight Loss in Cancer Patients

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Weight loss may be one of the presenting manifestations of cancer or it may appear as the disease advances. The tissues and organs that lose weight in cancer patients also deteriorate during starvation. The primary exception is the liver, which loses weight in starving patients but gains weight in those with cancer. Although the pathogenesis remains unexplained, this observed increase in dry liver weight is absolute, rather than relative, and secondary to the decreased carcass weight of the host.

Why do patients with cancer lose weight? In general, weight loss develops because of a negative balance between intake and expenditure of calories. Such a negative balance may occur with decreased calorie intake and normal energy expenditure, with normal calorie intake but increased energy spending, or with decreased calorie intake and increased calorie expenditure. At the clinical level, an imbalance can result from: (1) inadequate food ingestion; (2) impaired digestion and absorption; (3) external nutrient loss; (4) tumor-host competition for nutrients; or (5) increased energy expenditure of the host. In the cancer patient, all these abnormalities may occur singly or in combination, thereby contributing to weight loss and eventually to the development of cachexia, the hallmark of cancer.

Inadequate Food Ingestion

Anorexia and early satiety are present in 40 percent of cancer patients at the time of initial recurrence or spread of disease. These symptoms are the main reasons for decreased food ingestion. The oligophagia increases in magnitude and severity with progression of the cancer and institution of therapy, in turn causing anorexia or early satiety at sometime during the course of the disease in almost every cancer patient.

Anorexia is primarily caused by the cancer itself. It has been postulated that the disease produces anorexia-inducing intermediary metabolites, such as peptides and other small molecules, that perturb central and peripheral food intake regulatory mechanisms.

Following the diagnosis of cancer, psychological and emotional disturbances—depression, anger, anxiety and grief—may unfavorably affect the appetite and cause a drop in food consumption. Abnormalities of taste due to the cancer or its treatment, namely radiotherapy or chemotherapy, might also contribute to anorexia. Furthermore, patients with cancer frequently com-
plain that the smell of food has changed and become unpleasant. However, as no critical studies are available on olfactory disturbances related to the development, growth and treatment of cancer, it is not known to what extent such changes contribute to a decreased food intake.

Anorexia may also be observed in patients with extensive hepatic involvement or severe hepatotoxicity from prolonged use of certain antineoplastic agents, such as methotrexate. Cancer located in the oro-pharynx, the esophagus, the stomach or the small intestine may impair function and interfere with ingestion.

As stated, surgery, radiotherapy and chemotherapy may also affect food ingestion. Partial or total glossectomy and mandibulectomy may hinder mastication and deglutition, while esophagectomy and gastrectomy may lower food intake. Radiotherapy and chemotherapy frequently cause nausea and occasionally vomiting. Irradiation to the head and neck may induce xerostomia, dental deterioration, oropharyngitis and esophagitis with difficulties in chewing, painful swallowing and dysphagia; chemotherapy may cause stomatitis, pharyngitis and esophagitis.

Nausea, discomfort or pain during or after eating may lead to a conditioned aversion to eating, which may persist even after the causative factor has been removed or alleviated. Behavior modification therapy may be required.

The end result is oligophagia. The patient, by failing to ingest enough nutrients, fails to meet his energy needs and develops a negative energy balance. However, as has been demonstrated by forced feeding, paired feeding and caloric restriction experiments in tumor-bearing animals, the decreased food intake alone cannot entirely account for progressive weight loss.

Impaired Digestion and Absorption

Patients with cancer may develop some degree of impaired small intestinal function with malabsorption, even when the neoplasm exists outside the alimentary tract. A partial villous atrophy of the jejunal mucosa has been observed in these patients.

Cancer of the stomach may cause digestive disturbances. Extensive replacement of the pancreas with tumor and involvement of the pancreatic duct or common bile duct may affect secretion of pancreatic juices and bile, thus interfering with digestion and absorption, especially of fats and fat soluble substances. Moreover, infiltration of the small intestine with lymphoma or solid tumor, or significant mesenteric lymphadenopathy and lymphedema of the intestinal wall may lead to malabsorption of various nutrients. Ascites may also disturb intestinal function and absorption.

Malabsorption may further result from alimentary tract surgery: esophageal resection with vagotomy may cause steatorrhea; gastrectomy is often followed by postgastrectomy malabsorption syndromes; resection of jejunum or ileum may lead to inadequate absorption of certain nutrients, depending on the area removed. Gastrocolic or enterocolic fistulae may cause nutrients to bypass large segments of the small intestine, while a blind loop syndrome created by gastrointestinal surgery may result in impaired absorption of certain substances.

Radiation to the abdomen and pelvis may cause acute or late enteritis in the irradiated segments; it may also indirectly affect the bowel through endarteritis of the small intestinal vessels. The resulting complications, such as mucosal atrophy and flattened villi, fibrosis, stenosis, necrosis, ulcerations, hemorrhage, obstruction and fistula formation, may further alter intestinal physiology.

Antineoplastic agents that damage the rapidly proliferating gastrointestinal
epithelium may also cause injury of the bowel mucosa with ulcerations and infections, adversely affecting intestinal function. In addition, tumors may secrete a variety of potent pharmacologic substances causing increased intestinal motility and diarrhea, and resulting in malabsorption; the best known such clinical entities are the carcinoid and Zollinger-Ellison syndromes.\(^9\)

**External Nutrient Loss**

Protein-losing enteropathy has been observed in patients with lymphomas and solid tumors involving the small intestine; lipids are probably also lost in these patients. In those with a nephrotic syndrome, from a variety of etiologies, albumin may be lost in the urine. Significant albumin loss may also result from repeated therapeutic removal of malignant effusions. When cancer replaces the pancreas, glucosuria has been observed, but the total loss of glucose is not of great consequence in the development of weight loss.

**Tumor-Host Competition for Nutrients**

Competition for nutrients between the host and a more aggressive partner, the tumor, theoretically could create some nutritional disadvantages for the host. A selective nutrient uptake by the tumor, leading to a deficit in the patient, has been proposed, especially for certain vitamins, such as folic acid. It has been suggested that observed changes in amino acid patterns in the blood and tissues of the host may represent the tumor’s increased demand and selective removal of certain amino acids. Any such demand could theoretically deplete the respective amino acid and alter the metabolism of the host.\(^9\)

In general, chemical analyses of neoplasms have not shown an unusual concentration of any nutrient in the tumor, nor have metabolic studies demonstrated any excessive destruction of a particular substance, with the possible exception of large sarcomas consuming glucose and causing hypoglycemia in the host. Furthermore, it is difficult to imagine how a small tumor could drain enough nutrients to create a deficit for the host. Nevertheless, weight loss can be observed even with small tumors and occasionally in the presence of adequate food intake.\(^3\)

Theoretically, again, an adequate nutrient supply should be capable of replenishing the metabolic pool of the host and, even in the presence of a large tumor, meet the needs of both partners. This is the case in pregnancy where the host thrives in the presence of a rapidly growing fetus.

However, in cancer patients, even with forced feeding, an initially observed nitrogen retention is short-lived and transient, with a tendency for the nitrogen balance to rapidly approach equilibrium and then to move to a negative phase.\(^11\) Although the patient gains weight during forced feeding, analysis of the weight in terms of body compartments has revealed that the increase is predominantly due to an accumulation of large quantities of intracellular fluid, which are rapidly lost after discontinuing hyperalimentation.\(^11\)

It is clear, therefore, that weight loss in patients with cancer is not simply the result of semi-starvation and depletion of nutrients in the metabolic pool of the host, but a much more complex metabolic problem.

**Increased Energy Expenditure**

A significant increase in the basal metabolism rate could contribute to weight loss in the cancer patient. However, both the incidence and the degree of increased caloric expenditure in such patients remain controversial\(^12\) largely because of the limitations of those methods used to estimate energy metabolism in humans.

Following tumor transplantation in certain experimental cancers, a process
is initiated that definitely results in increased energy expenditure. The increase in total energy expenditure becomes apparent almost immediately after transplantation and before any tumor can be palpated.

In many cancer patients, the caloric expenditure is increased and, again, the quantity of malignant tissue does not appear to account for the increased values obtained. The cancer somehow induces the host to maintain a higher basal metabolism rate—concomitant infections and other complications may also contribute to the hypermetabolic state—and the patient must utilize adipose tissue and muscle mass as a source of metabolic fuel.

Decreased metabolic rates are usually found in healthy subjects when alimentation is decreased. In contrast, cancer patients may show increased oxygen consumption in the basal state despite falling caloric intake; it is very unusual to find lowered metabolic rates, even in the presence of marked decreases in food intake. Many of the adaptive mechanisms for energy conservation normally seen with semi-starvation appear impaired in the patient with uncontrolled cancer growth.

The pathogenesis of increased energy expenditure in the cancer patient remains hypothetical. There is ample evidence of major alterations of protein, lipid and carbohydrate metabolism in the host, resulting from the presence and growth of cancer; but in what way and to what extent these alterations contribute to a weight loss remains conjectural.

Management of Weight Loss

At present, the only effective way to reverse the weight loss is to cure or control the cancer. However, temporary reversal of weight loss may be achieved by preventing or managing complications, and by increasing the caloric intake of the anorectic patient by having him nibble a variety of highly nutritious foods rather than attempting to eat widely-spaced large meals. Parenteral hyperalimentation and elemental diets are also promising new approaches for the nutritional management of selected patients with advanced cancer.

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