

*ABC of palliative care***Anorexia, cachexia, and nutrition**

Eduardo Bruera

Cachexia is a complex syndrome that combines weight loss, lipolysis, loss of muscle and visceral protein, anorexia, chronic nausea, and weakness. Severe cachexia occurs in most patients with advanced cancer or AIDS. This article covers approaches to cachexia other than treatment of the underlying disease. In those patients who are eligible for tumouricidal treatment, cachexia may resolve as the disease responds.

When faced with a cachectic patient, the clinician may approach the problem with four questions:

- Does the patient have cachexia?
- Why is the patient cachectic?
- Which treatments are effective?
- How should treatment be individualised?

Does the patient have cachexia?**Frequency of cachexia**

More than 80% of patients with cancer or AIDS develop cachexia before death. At the moment of diagnosis, about 80% of patients with upper gastrointestinal cancers and 60% of patients with lung cancer have substantial weight loss. In general, patients with solid tumours (with the exception of breast cancer) have a higher frequency of cachexia. Cachexia is also more common in children and elderly patients and becomes more pronounced as disease progresses.

Assessing nutritional status

Because of the chronic nature of cancer cachexia, the diagnosis is simple. A patient's clinical history, the presence of substantial weight loss, and physical examination are adequate for an accurate diagnosis.

Plasma albumin concentration is usually decreased. Simple bedside measurements—such as triceps or subscapular skin folds (for body fat) and arm muscular circumference (for body lean mass)—may be useful to monitor nutritional changes or the effect of treatments in patients in whom body weight might be unreliable (such as those with ascites or oedema).

More sophisticated laboratory investigations are usually unnecessary. Immunological tests are unreliable markers of nutritional status in patients with cancer or AIDS because of the immunological abnormalities due to the underlying illness.

Why is the patient cachectic?

While metabolic abnormalities are the main cause of malnutrition, decreased caloric intake and malabsorption also contribute to the cachexia syndrome.

Decreased caloric intake

Anorexia is an almost universal component of cachexia. Reduced caloric intake may be more severe in patients with dysphagia due to head and neck pain or oesophageal carcinoma, psychological depression, abnormalities of taste, or chronic nausea. The last is a common symptom in malignant diseases and can be due to autonomic failure, opioids and other drugs, constipation, or bowel obstruction.



Patient with cachexia

Effects of cachexia

- Decreased survival
- Increased complications of surgery, radiotherapy, and chemotherapy
- Weakness, anorexia, chronic nausea
- Psychological distress in patient and family

In most patients cachexia is caused by metabolic abnormalities due to the production of tumour products and cytokines by the immune system. Anorexia is a major contributor to cachexia in a minority of patients, but in most it is simply a symptom of cachexia

Metabolic abnormalities

Traditionally, cancer was assumed to cause cachexia by consuming energy and by releasing factors capable of causing anorexia. This interpretation justified aggressive nutrition as an approach to restore the energy balance.

The emerging view is that cachexia of cancer is mainly due to major metabolic abnormalities. These are caused predominantly by cytokines released by the immune system as a response to the presence of the cancer (cachectin-tumour necrosis factor and interleukins 1 and 6) and are probably also related to the cachexia of other diseases such as AIDS, tuberculosis, and leprosy.

Tumour products have also been identified (such as lipolytic hormones). These factors cause profound lipolysis, negative nitrogen balance, and anorexia. In most patients, anorexia is more likely the result of the catabolic process rather than the cause of the cachexia. This view explains the failure of aggressive nutrition in changing clinical outcome, symptoms, and the nutritional status of cancer patients.

Malabsorption

This should be suspected in patients with pancreatic insufficiency due to pancreatic or other gastrointestinal cancers, or in patients who have recently received aggressive radiation therapy to the abdomen. It is an uncommon cause of malnutrition.

Which treatments are effective?

Weight loss is an independent risk factor for poor survival. Cachectic patients have a higher incidence of complications after surgery, radiotherapy, and chemotherapy. In addition, cachexia aggravates weakness, is associated with anorexia and chronic nausea, and is a source of psychological distress for patients and families because of the associated symptoms and the changes in body image. This prompts some to attempt aggressive nutritional supplementation.

Advantages of intensive nutrition

The complications of cachexia and the view that it results mostly from an energy deficit has generated many studies attempting to reverse these complications with total parenteral or enteral nutrition. Unfortunately, these studies have generally found no significant improvement in patient survival or tumour shrinkage, and limited effects on the complications associated with surgery, radiotherapy, or chemotherapy. Since most studies failed to assess patients' symptoms it is not clear if intensive nutrition confers any symptomatic benefits.

However, intensive nutrition is appropriate in certain clinical situations, such as in patients recovering from surgery and awaiting chemotherapy. When selecting patients for nutrition, doctors must take into account the morbidity (15% in some studies) and the financial cost.

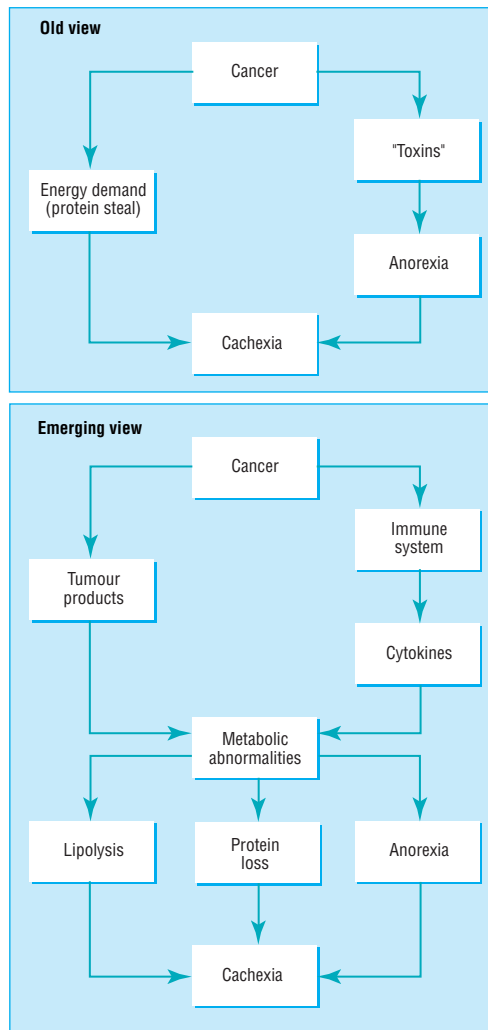
Effects of pharmacological management

Several drugs have beneficial effects on the symptoms of cachexia, and some have effects on patients' nutritional status.

Corticosteroids

These improve both anorexia and weakness in cancer patients. However, these effects are purely subjective and are not accompanied by any important improvement in caloric intake or nutritional status. The effects are usually short lasting (limited to 3-4 weeks), but they are usually well tolerated for brief periods even in very ill patients.

Probable causes of cachexia



Traditional and emerging views of causes of cancer cachexia

Therapeutic options

- Dietary advice
- Nutritional supplementation
- Prokinetic drugs
- Corticosteroids
- Progestational drugs
- Tumouricidal treatment (if appropriate)

An identifiable and reversible cause of weight loss is an indication for intensive nutrition

Effects of intensive nutrition

- No increase in survival
- No improved tumour shrinkage
- Minimal decrease in toxicity of chemotherapy or radiotherapy
- Minimal decrease in surgical morbidity
- Unknown symptomatic effects

The mechanism of action is unknown but is possibly related to inhibition of the release of metabolic products by the tumour or immune system or to a non-specific central euphoriant effect.

Corticosteroids also have antiemetic and other effects, including analgesia, improvement in neurological symptoms due to cerebral oedema and spinal cord or nerve compression, decrease in breathlessness due to lymphangitis carcinomatosa, and anecdotal reports of a beneficial effect on the symptoms associated with bowel and ureteral obstruction.

Progestational drugs

Medroxyprogesterone and megestrol acetate may substantially improve appetite, caloric intake, and nutritional status in patients with advanced cancer or AIDS. These drugs also result in an increased deposition of fat. Controlled trials have shown that megestrol acetate improves several symptoms in addition to appetite, including a sensation of wellbeing, reduced fatigue, and some aspects of quality of life. When used as an appetite stimulant, megestrol acetate has no effect on survival of patients with cancer or AIDS.

The progestational drugs' mechanism of action is unclear. Since intensive nutrition has limited nutritional effects and no obvious symptomatic advantages, it is unlikely that both the subjective and objective effects of megestrol acetate are due to increased appetite and caloric intake. More likely, these drugs have an effect on the metabolic abnormalities due to the cancer, and the increase in appetite is secondary to reversal of the catabolic state. The main drawback of progestogens is their high cost and side effects such as oedema and thrombotic episodes.

Prokinetic agents

These can have a considerable effect on symptoms in patients complaining of anorexia accompanied by early satiety or chronic nausea. Such symptoms are mostly due to gastroparesis because of autonomic failure, brought on by the presence of the cancer or malnutrition, or the effect of drugs such as opioids or tricyclic antidepressants.

Other drugs

Other drugs are thought to have effects on appetite, but the evidence is anecdotal and clinical use is not justified at this time. Clinical trials are being conducted on cyproheptadine, oxpentifylline, melatonin, thalidomide, certain cannabinoids, and low doses of alcohol.

Hydrazine sulfate has had publicity in north America and is used widely as an "alternative" drug for cancer cachexia. Three recent randomised controlled trials have found it no more effective than placebo with regards to nutritional status, survival, symptoms of cachexia, or quality of life. In addition, it causes considerable toxicity, including peripheral neuropathy.

Individualising treatment

Determining expectations and outcomes

It is extremely important to establish initially what patients, their family, and their physician expect from any treatment. Neither nutritional nor drug treatments confer any survival advantage in metastatic cancer. Intensive nutritional replacement has limited, if any, value for patients with advanced and progressive disease; exceptions may include head and neck tumours that advance locally but metastasise slowly and neurological disorders such as motor neurone disease.

Although megestrol acetate and, in some cases, artificial nutrition provide nutritional improvement, this alone does not justify treatments that are potentially toxic for terminally ill patients unless there is a substantial benefit to quality of life.

Choices of drug management of cachexia

Corticosteroids

- Dexamethasone, methylprednisolone, prednisolone, and hydrocortisone have been found to be effective
- Optimal dose is unknown, but equivalent daily doses of prednisolone 40 mg (dexamethasone 6 mg) are used most often
- Dexamethasone can be given subcutaneously

Progestational drugs

- Medroxyprogesterone and megestrol acetate
- Dose finding studies suggest the starting dose of megestrol acetate should be 480 mg a day (three times the antineoplastic dose)
- There is some evidence for using a combination of megestrol acetate and ibuprofen for cancer cachexia

Prokinetic drugs

- Metoclopramide is most widely used, at doses of 10-20 mg taken 30 minutes before meals or 30-80 mg as a continuous subcutaneous infusion
- Domperidone or cisapride are appropriate alternatives



The size and appearance of meals may be as important as their nutritional value. Standard hospital meals (top) are generally unsuitable and should be replaced by smaller, more attractive helpings (bottom)

Outcome measures of treatment

Traditional outcome measures

- Survival
- Tumour response
- Treatment toxicity
- Nutritional status

Palliative outcome measures

Improvement in

- Anorexia and weakness
- Other symptoms
- Patient's or family's satisfaction
- Functional status
- Nutritional status

Choice of treatment

Nutritional counselling should be based on eating high calorie meals of small portions that are pleasant for the patient. It is important to include the patient's family in such discussions. It is useful to clarify that an excess of calories is unlikely to benefit the patient by explaining that his or her metabolic system does not have the ability to use these calories in the same way as that of a healthy person. Although cachectic, the patient is not "starving."

Patients who are unable to swallow because of severe dysphagia (for example, because of head and neck or oesophageal cancers and neurological disorders) and who complain of hunger or express concerns related to malnutrition may benefit from nutrition via a gastrostomy tube. Such tubes can be inserted with ultrasonographic or endoscopic guidance.

Patients with chronic nausea, early satiety, or other findings suggesting gastroparesis should receive a trial of a prokinetic drug. Patients with slowly progressive illness for whom anorexia is an important symptom may benefit from both the symptomatic and nutritional effects of megestrol acetate. Severely ill patients with multiple complex symptoms and a limited life expectancy are more likely to benefit from the multiple symptomatic effects of a course of corticosteroids. Finally, patients for whom anorexia is a relatively minor problem or those who are severely cognitively impaired may not require any treatment.

In patients with mechanical bowel obstruction, prokinetic drugs may aggravate emesis. Antiemetics, octreotide, hyoscine, or nasogastric drainage will be required for symptom relief. Some special conditions may further reduce food intake and require assessment and management; these include chemotherapy or radiotherapy induced mucositis or emesis and severe depression.

Future developments

Clinical trials are currently being conducted on drugs with a subjective effect on appetite and energy, anabolic agents, and drugs capable of inhibiting the release of cachectin-tumour necrosis factor. Differential nutrition with amino acids and fatty acids capable of influencing the metabolic response of the tumour are also being investigated.

Choosing treatments for cachexia

- Intensive nutrition is expensive, associated with morbidity, and there is limited evidence that it can reverse these problems
- Corticosteroids and megestrol acetate are effective appetite stimulants. The weight gain associated with megestrol acetate takes some weeks to manifest
- Prokinetic drugs may improve nausea and early satiety
- The psychological aspects of cachexia can be the most important for patients and their carers. Feeding a dependant is the essence of nature and this fundamental breakdown must be addressed. Explanations and practical solutions are often more important than any drugs administered



Percutaneous endoscopic gastrostomy

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The ABC of palliative care is edited by Marie Fallon, Marie Curie senior lecturer in palliative medicine, Beatson Oncology Centre, Western Infirmary, Glasgow, and Bill O'Neill, science and research adviser, British Medical Association, BMA House, London. It will be published as a book in June 1998.

A paper that changed my practice A lesson in time management

In the 1950s, when I was a student at Harvard University, long before I embarked on a medical career, I read the women's pages in the *Boston Globe* regularly. The section was devoted to homemaking and was chockful of news, articles, and advice about housekeeping, meal preparation, childcare, and gardening. One piece of advice that I found there, and started to implement immediately, was the principle of "15 minutes a day."

Housewives who despaired of ever getting a particular disliked household task done would write in asking for advice. The columnist had a standard suggestion: set a limit of 15 minutes a day to work on it. At the end of 15 minutes a person could stop with a clear conscience, having accomplished what was planned, looking forward to working only 15 minutes more on the same chore the following day. As I frequently found it hard to start on a study session or a writing assignment, I decided to try the "15 minutes a day" approach. It was successful for me the very first time. After 15 minutes it was usually impossible to stop what I was doing. Very often I would wind up spending hours on an activity previously put off for hours, days, or even longer, despite knowing

well that it was important work that I was obliged to complete. But I started out limiting myself to 15 minutes.

I find it convenient to use a timer that rings. Sometimes I set it for 30 minutes or longer; I am now conditioned to begin work as soon as it starts up. The principle found in the women's pages decades ago has proved important to me in the years of my medical career, as well as in my personal life.

Elaine Ristinen, *physician in occupational and preventive medicine, New York*

We welcome filler articles up to 600 words on topics such as *A memorable patient, A paper that changed my practice, My most unfortunate mistake*, or any other piece conveying instruction, pathos, or humour. If possible the article should be supplied on a disk. Permission is needed from a patient or a relative if an identifiable patient is referred to. We also welcome contributions for "Endpieces," consisting of quotations of up to 80 words (but most are considerably shorter) from any source, ancient or modern, which have appealed to the reader.